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Local Irritation Toxicity Study of Hypertonic Saline/Dextran 70® and Constituents in New Zealand White Rabbits

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**MAMMALIAN TOXICOLOGY BRANCH
DIVISION OF TOXICOLOGY**

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Toxicology Series 244

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Local Irritation Toxicity Study of Hypertonic Saline/Dextran 70® and Constituents in New Zealand White Rabbits (Toxicology Series 244)--Zaucha *et al*

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In conducting the research described in this report, the investigation adhered to the "Guide for the Care and Use of Laboratory Animals," as promulgated by the Committee on Revision of the Guide for Laboratory Animal Facilities and Care, Institute of Laboratory Animal Resources, National Research Council.

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Edwin S. Beatrice 19 Dec 88

**Edwin S. Beatrice
COL, MC
Commanding**

(date)

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19. ABSTRACT (cont.)

high incidence of hematoma and bruise formation was observed at the intra-arterial sites (0.2 ml), but these changes were distributed equally among the four dosing solutions. No clinical signs were observed at the intramuscular injection sites (0.5 ml). Only transient injection bleb formation was observed at the subcutaneous sites (0.5 ml). The clinical observations following injection of the test substances were attributed to the perivascular leakage of blood subsequent to needle insertion. Designated subsets of the animals were submitted for necropsy at 4, 24, 48, and 72 hours after the injections for gross and microscopic evaluation of the injection sites. The pathologic findings were also consistent with leakage associated with needle insertion, and were of minimal clinical significance. These results suggest that hypertonic saline/dextran and its constituents are no more irritating than Ringer's lactate when administered by intravenous, paravenous, intra-arterial, intramuscular, or subcutaneous injection.

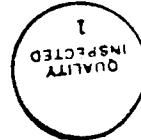
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ABSTRACT

The potential for local irritation following intravenous, paravenous, intra-arterial, intramuscular, and subcutaneous injections of hypertonic saline/Dextran 70® was evaluated with solutions of its major constituents, hypertonic saline (7.5%) and Dextran 70® (6%) in normal saline, in male New Zealand White rabbits. Ringer's lactate was also evaluated as a control. Animals were observed for signs of local irritation at 4, 24, 48, and 72 hours after the injections. Intravenous injections (0.5 ml) of hypertonic saline or Dextran 70® resulted in an increased incidence of bruises at the injection site relative to injections of hypertonic saline/Dextran 70® and Ringer's lactate. Paravenous injection (0.1 ml) resulted in the transient formation of injection blebs by all 4 dosing solutions and isolated bruising at the hypertonic saline, hypertonic saline/Dextran 70®, and Dextran 70® sites. A high incidence of hematoma and bruise formation was observed at the intra-arterial sites (0.2 ml), but these changes were distributed equally among the four dosing solutions. No clinical signs were observed at the intramuscular injection sites (0.5 ml). Only transient injection bleb formation was observed at the subcutaneous sites (0.5 ml). The clinical observations following injection of the test substances were attributed to the perivascular leakage of blood subsequent to needle insertion. Designated subsets of the animals were submitted for necropsy at 4, 24, 48, and 72 hours after the injections for gross and microscopic evaluation of the injection sites. The pathologic findings were also consistent with leakage associated with needle insertion, and were of minimal clinical significance. These results suggest that hypertonic saline/dextran and its constituents are no more irritating than Ringer's lactate when administered by intravenous, paravenous, intra-arterial, intramuscular, or subcutaneous injection.

Key Words: Local Irritation, Intravenous Injection, Paravenous Injection, Intra-arterial Injection, Intramuscular Injection, Subcutaneous Injection, Hypertonic Saline/Dextran 70®, Hypertonic Saline, Dextran 70®, New Zealand White Rabbits

PREFACE

TYPE REPORT: Local Irritation Toxicity GLP Study Report

TESTING FACILITY:

US Army Medical Research and Development Command
Letterman Army Institute of Research
Presidio of San Francisco, CA 94129-6800

SPONSOR:

US Army Medical Research and Development Command
Letterman Army Institute of Research
Presidio of San Francisco, CA 94129-6800

PROJECT DIRECTOR: Charles Wade, PhD

PROJECT/WORK UNIT/APC: 3S463807D836/087/TLRO

GLP STUDY NUMBER: 88004

STUDY DIRECTOR: Don W. Korte, Jr., PhD, MAJ, MSC
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PRINCIPAL INVESTIGATOR: Gary M. Zaucha, DVM, CPT, VC

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Diplomate, American College of
Veterinary Preventive Medicine

PATHOLOGIST: G. David Young, DVM, MAJ, VC

DATA MANAGER: Yvonne C. LeTellier, BS

REPORT AND DATA MANAGEMENT: A copy of the final report,
study protocols, retired SOPs,
raw data, analytical and
stability data, and an aliquot
of the test compound will be
retained in the LAIR Archives.

TEST SUBSTANCE: Hypertonic Saline/Dextran 70®

INCLUSIVE STUDY DATES: 21 Apr 88 - 10 Jun 88

OBJECTIVE: The objective of this study was to determine
the local irritation potential of hypertonic
saline/Dextran 70® in male New Zealand White
Rabbits.

ACKNOWLEDGMENTS

SPC Dean K. Magnuson, BS, SPC Eric Dahlberg, BS, and SPC Vilmar O. L. Villa provided assistance in dose preparation and administration; SGT Tammie Heineman, SGT Barbara D. Green, and Richard Katona provided data collection, animal care, and facility management; and Synitha Fuller provided secretarial assistance.

SIGNATURES OF PRINCIPAL SCIENTISTS AND MANAGERS
INVOLVED IN THE STUDY

We, the undersigned, declare that GLP study number 88004 was performed under our supervision, according to the procedures described herein, and that this report is an accurate record of the results obtained.

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DEPARTMENT OF THE ARMY

LETTERMAN ARMY INSTITUTE OF RESEARCH
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REPLY TO
ATTENTION OF

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13 December 1988

MEMORANDUM FOR RECORD

SUBJECT: GLP Compliance for GLP Study 88004

1. This is to certify that in relation to LAIR GLP Study 88004, the following inspections were made:

27 January 1988	- Protocol Review
11 May 1988	- Animal Receipt/Room Inspection
07 June 1988	- Dosing
07 June 1988	- Necropsy (4-Hour)
08 June 1988	- Observations & Weighing
13 June 1988	- Histology

2. The institute report entitled "Local Irritation Toxicity Study of Hypertonic Saline/Dextran 70 and Constituents in New Zealand Rabbits," Toxicology Series 244, was audited on 21 November 1988.

Carolyn M. Lewis

CAROLYN M. LEWIS, MS
Diplomate, American Board of Toxicology
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TABLE OF CONTENTS

	Page
Abstract.....	i
Preface.....	iii
Acknowledgments.....	iv
Signatures of Principal Scientists.....	v
Report of Quality Assurance Unit.....	vi
Table of Contents.....	vii
INTRODUCTION.....	1
Objective of Study.....	1
MATERIALS.....	2
Test Substance.....	2
Test Substance Constituents.....	2
Control.....	3
Animal Data.....	3
Husbandry.....	3
METHODS.....	4
Group Assignment/Acclimation.....	4
Dose Levels, Preparation, and Analysis.....	4
Test Procedures.....	4
Observations.....	6
Necropsy.....	6
Statistical Analysis.....	6
Duration of Study.....	6
Changes/Deviations.....	6
Storage of Raw Data and Final Report.....	7
RESULTS.....	7
Clinical Observations.....	7
Body Weights.....	8
Necropsy Findings.....	8
DISCUSSION.....	13
CONCLUSION.....	13

TABLE OF CONTENTS (continued)

	Page
REFERENCES.....	14
APPENDICES.....	16
Appendix A. Chemical Data.....	17
Appendix B. Animal Data.....	21
Appendix C. Historical Listing of Events.....	22
Appendix D. Individual Animal Histories.....	24
Appendix E. Individual Body Weights.....	49
Appendix F. Pathology Report.....	51
OFFICIAL LIST OF DISTRIBUTION.....	112

Local Irritation Toxicity Study of Hypertonic
Saline/Dextran 70® and Constituents in New Zealand
White Rabbits -- Zaucha et al

INTRODUCTION

During conventional land warfare it has been estimated that 90% of the deaths occur either in the field or en route to a fixed medical treatment facility and that 50% of those deaths occur due to hemorrhage (1). Conventional treatment of hemorrhage has involved infusion of isotonic resuscitation fluids at volumes equivalent to two or three times the volume of blood lost (2). Supplying this volume of resuscitation fluid on the battlefield for treatment of multiple casualties is not feasible.

Hypertonic crystalloid solutions have been used for the past 70 years in the treatment of hemorrhage (3). However, the consensus has been that unless followed by replacement of the lost blood volume, the beneficial effects of treatment with hyperosmotic solutions are transient (4). Recently, the addition of a hyperoncotic colloid, 6% Dextran 70®, to the hypertonic crystalloid, 7.5% saline, has significantly extended 96-hour survival rates compared with those obtained with normal saline or 7.5% saline (5). If the effectiveness of this hypertonic saline/Dextran therapy is verified by clinical trial, it would be a significant advance in the treatment of blood loss due to traumatic injuries.

As with any new treatment regimen, there are potential risks. Low molecular weight dextran may cause bleeding abnormalities and phlebitis or interfere with the cross-matching of blood (6). Hypertonic solutions may cause neurologic abnormalities induced by the rapid increases in osmolalities (7-9) or cardiac arrhythmias induced by the hypokalemia associated with the rapid expansion of extracellular space (2, 10). Consequently, the Division of Toxicology, Letterman Army Institute of Research, was tasked to provide an acute and subchronic toxicity profile of the 7.5% hypertonic saline/6% Dextran 70® resuscitation fluid (HSD). This report describes the results of a local irritation study of HSD in male New Zealand White rabbits.

Objective of Study

The objective of this study was to determine the local irritation potential of hypertonic saline/Dextran 70® in male New Zealand White rabbits.

MATERIALS

Test Substance

Name: Hypertonic saline/Dextran 70®

LAIR Compound Code: TP96

Lot Number: NC 54845

Expiration Date: 31 December 1988

Composition per 100 ml: Dextran 70® 6 g
sodium chloride 7.5 g
water for injection to 100 ml

Source: Pharmacia LEO Pharmaceuticals
Uppsala, Sweden

Test Substance Constituents

Name: Hypertonic saline (7.5%)

LAIR Compound Code: TP98

Lot Number: I 318712

Expiration Date: 31 December 1988

Composition per 100 ml: sodium chloride 7.5 g
water for injection to 100 ml

Source: Pharmacia LEO Pharmaceuticals
Uppsala, Sweden

Name: Dextran 70®

LAIR Compound Code: TP95

Lot Number: NE 54941

Expiration Date: 31 May 1989

Composition per 100 ml: Dextran 70® 6 g
sodium chloride 0.9 g
water for injection to 100 ml

Source: Pharmacia LEO Pharmaceuticals
Uppsala, Sweden

Control

Name: Ringer's lactate

LAIR Compound Code: TP97

Lot Number: NC 54847

Expiration Date: 31 December 1988

Composition per 100 ml:	sodium chloride	600 mg
	potassium chloride	30 mg
	calcium chloride	
	dihydrate	20 mg
	sodium lactate	310 mg
	water for injection to 100 ml	

Source: Pharmacia LEO Pharmaceuticals
Uppsala, Sweden

Other test substance information is presented in
Appendix A.

Animal Data

Twenty-six male New Zealand White rabbits (Elkhorn Rabbitry, 5265 Starr Way, Watsonville, CA 95076) were assigned to this study. They were identified individually with neck bands (E-Jay International Inc., P.O. Box 1835, Glendora, CA 91740). Two of the rabbits were utilized for quality control necropsy. The animal weights on receipt ranged from 2.0 to 2.6 kg. Additional animal data appear in Appendix B.

Husbandry

Study animals were individually housed in stainless steel, battery-type cages with screened bottoms, in racks equipped with automatically flushing dump tanks. The diet, fed at approximately 150 g per day (refilled each morning), consisted of Certified Purina® Rabbit Chow 5322 (Ralston Purina Company, St. Louis, MO); water, purified by reverse osmosis, was provided by continuous drip from a central line. The animal room temperature and humidity were continuously monitored by hygrothermograph. The temperature was maintained in a range from 20.0°C to 25.6°C, with a relative humidity range of 27 to 65%, with occasional spikes to as high as 84% during room cleaning. The photoperiod was 12 hours of light per day (0600 - 1800 hours).

METHODS

This study was conducted in accordance with FDA guidelines (11) and LAIR SOP-OP-STX-114, "Local Irritation Bioassay" (12).

Group Assignment/Acclimation

Since animals were to be terminated at four different time intervals following dosing, they were randomized into four groups of 6 animals each. Each group was further divided into 2 subgroups (a & b) of 3 animals each. Allocation was accomplished using a computer-based, stratified, weight-biased method. The XYBION Path/Tox AESLCT Animal Allocation Program was used in conjunction with a VAX 750 Computer.

The study animals were acclimated for 46 days before the day of dosing. During this period they underwent a 10 day treatment of sulfquinuoxaline in the drinking water for coccidiosis, were checked daily for signs of illness, and weighed weekly.

Dose Levels, Preparation, and Analysis

The local irritation potential following intravenous, paravenous, intra-arterial, intramuscular, and subcutaneous injections for 2 of the 4 intravenous formulations was evaluated in each animal, 1 solution being injected on the right side and 1 solution on the left (Table 1). The following dose levels were used: intravenous, 0.5 ml at a rate of 0.1 ml/10 seconds; paravenous, 0.1 ml in 10 seconds; intra-arterial, 0.2 ml at a rate of 0.1 ml/10 seconds; intramuscular, 0.5 ml in 10 seconds; and subcutaneous, 0.5 ml in 10 seconds. Solutions were used as supplied by the manufacturer, Pharmacia LEO Pharmaceuticals. Analysis of the dosing solutions was provided by Pharmacia LEO Pharmaceuticals. Additional chemical data are presented in Appendix A.

Test Procedures

The potential for local irritation of hypertonic saline/Dextran 70® (HSD) was evaluated in parallel with solutions of its major constituents, hypertonic saline (HS, 7.5%) and Dextran 70® (DEX 70, 6%) in normal saline, with Ringer's lactate (LRS) serving as the control. The dosing solutions were administered at the following injection sites: intravenous via the marginal ear vein as close to the tip of

Table 1
DOSE GROUPS

Group	Right Side	Left Side
4-hr sacrifice		
1a	HSD	Ringer's lactate
1b	hypertonic saline	Dextran 70®
24-hr sacrifice		
2a	HSD	Ringer's lactate
2b	hypertonic saline	Dextran 70®
48-hr sacrifice		
3a	HSD	Ringer's lactate
3b	hypertonic saline	Dextran 70®
72-hr sacrifice		
4a	HSD	Ringer's lactate
4b	hypertonic saline	Dextran 70®

the ear as feasible, paravenous immediately medial to the marginal ear vein approximately 1 inch proximal to the intravenous site, intra-arterial via the central artery of the ear near the base of the ear, intramuscular in the lateral compartment of the thigh (*m. vastus lateralis*), and subcutaneous in the dorsolateral thoracic region immediately caudal to the scapula. The hair on the injection sites was clipped with Oster clippers (Oster model A5, size 40 blade, Sunbeam Corporation, Milwaukee, WI 53217) on the day before dosing. Injections were made using tuberculin syringes (Becton Dickinson & Co., Rutherford, NJ 07070, Lot No. 7H355) and 23-gauge, 3/4-inch needles (manufactured by Nipro Medical Industries LTD., Tokyo, Japan, for Philadelphia Biologics Center, 1015 Chestnut Street, Philadelphia, PA 19107, Lot No. 82H31G). A 12-inch length of PE-50 polyethylene tubing (Clay Adams, Division of Becton Dickinson & Co., Parsippany, NJ 07054, Lot No. 93131, exp. date 6/92) was used to attach a second, hubless needle to the needle on the syringe to facilitate completion of the intravascular injections. Immediately following the injection, digital pressure was

Procedure

application of the adhesive tape around each injection site was made with indelible ink.

Observation

Observations were made immediately after all injections were completed and then at least twice daily for the remainder of the period. Clinical observations were accomplished on days 1, 2, 3, 6, 12, 18, 21, 24, 48, and 72 hours after the injections, recorded upon receipt of the animals, during the quarantine and observation period, and at necropsy. Gross and microscopic examinations of the injection sites and adjacent tissue.

Necropsy

Within one hour after sacrifice, all animals were submitted for necropsy. Immediately after sacrifice by barbiturate overdose, animals in Group 1 were submitted for necropsy 4 hours after completion of the injections, Group 2 was submitted to necropsy 24 hours after the injections, Group 3 was submitted to necropsy 48 hours after the injections, and Group 4 was submitted 72 hours after the injections.

Statistical Analysis

Clinical signs were tabulated by groups. The means and standard errors for the body weights for each group were calculated. The body weight data was subjected to a one-way analysis of covariance using dosing weight as the covariate and dose group as the factor of interest for each sacrifice day (13). Gross and microscopic pathology findings were described for each animal and tabulated by groups.

Duration of Study

Appendix C is a complete listing of historical events.

Changes/Deviations

Due to the short duration of the study and the need to keep the animals' ears free of extraneous marks, study animals were identified by neck bands rather than by ear tattoo.

Body weight determinations scheduled for 6 June 1988 were performed on 7 June 1988.

Coccidiosis was diagnosed during the quarantine period (13 May 1988). A 0.1% solution of sulfquinuoxaline (MSD AG Vet, Division of Merck Co., Inc., Lot No. EZA-715) in the drinking water was administered from 13 May 1988 to 22 May 1988 to all study animals.

Group 1a (HSD right side and LRS left side) had only 2 animals instead of 3 because animal 88F00114 died on 5 Jun 88, 2 days prior to dosing.

The area around each injection site was marked with ink immediately after completion of each injection rather than at the time of shaving of the sites.

It is believed that these changes had no adverse effects on the results of this study.

Storage of Raw Data and Final Report

A copy of the final report, study protocol, raw data, retired SOPs, and an aliquot of the test compound will be retained in the Letterman Army Institute of Research Archives.

RESULTS

Clinical Observations

The clinical observations included bruises, hematomas, subcutaneous blebs, nodules, and erythema of the injection sites.

The most frequently observed sign at the intravenous injection site was the presence of bruises (18 of 46). The greatest incidence of bruising was observed at the HS and DEX 70 sites (7 of 12 and 5 of 12, respectively). Bruises developed within 24-48 hours and appeared to decrease in size over time. Hematomas were observed at the HS and DEX 70 sites (1 of 12 and 2 of 12, respectively) 4 hours after injection. The hematomas resolved into bruises by 24 hours.

The most frequently observed sign at the paravenous injection site was the presence of injection blebs (6 of 46) immediately following injection. The majority of blebs resolved within 4 hours without residual effects. Bruising was observed at the HS, HSD, and DEX 70 sites (2 of 12, 1 of 11, and 1 of 12, respectively). The majority of the bruises

were observed by 24 hours. The persistence of bruising did not appear to be compound related.

Bruising was observed at the intra-arterial sites (37 of 46) with no equal distribution among dosing schedules. Bruising was observed immediately following injection in 10 of 37 animals and bruising, with 5 of 37 occurring at 24 hours. Bruising was observed at three animals receiving the 10 mg/kg dose. All bruising was resolved by 48 hours. Bruising was observed by 4 hours after dosing (24 of 37). The incidence of bruising was not compound related. In one animal two cases of indurated nodule formation were noted at the intra-arterial sites. The nodules were evaluated at 72 hours and were formed as a result of the resolution of bruising. The presence of nodules could not be correlated to a specific dosing solution. One incidence of bruising was observed in the LSF group.

No clinical signs were observed at the intramuscular injection sites.

Injection blebs were observed at the subcutaneous injection sites (14 of 46) immediately following injection, with the majority being observed at the HS and DEX 70 sites (5 of 12 at each respective site). All blebs had resolved by 24 hours.

Table 2 contains a summary of clinical observations. Appendix D contains individual animal histories.

Body Weights

Animal body weights were not significantly ($p \leq 0.05$) affected by dosing. Table 3 presents the mean body weights by group. Appendix E contains individual weight tables.

Necropsy Findings

No gross or microscopic pathological lesions attributable to the test compound or its constituents were reported. The Veterinary Pathologist's report is presented in Appendix F.

Table 2
INJECTION SITE EVALUATION*

Time (hours)	HSD				LRS				HS				DEX 70					
	H	B	L	N	E	n	H	B	L	N	E	n	H	B	L	N	E	n
Intravenous																		
0	-	-	-	-	-	11	-	-	-	-	11	1	-	-	-	12	-	-
4	-	-	-	-	-	11	-	-	-	-	11	1	3	-	-	12	2	1
24	-	1	-	-	-	9	-	1	-	-	9	-	5	-	-	9	-	4
48	-	1	-	-	-	6	-	3	-	-	6	-	3	-	-	6	-	3
72	-	1	-	-	-	3	-	-	-	-	3	-	1	-	-	3	-	-
Incidence\$-	3	-	-	-	-	11	-	3	-	-	11	1	7	-	-	12	2	5
																	-	12

* Clinical Observation Key
Values indicate incidence of observed sign.

H = hematoma

B = bruise

L = bleb

N = nodule

E = erythema

n = number of animals in group

\$ = total number of injection sites exhibiting the sign at least once during the study period.

Table 2 (cont.) : INJECTION SITE EVALUATION

Time (hours)	H	B	L	N	E	n	LRS						MS						DFX 70						
							H	B	L	N	E	n	H	B	L	N	E	n	H	B	L	N	E	n	
Intramuscular																									
0	-	-	-	-	-	11	-	-	-	-	11	-	-	-	-	-	-	12	-	-	-	-	-	12	
4	-	-	-	-	-	11	-	-	-	-	11	-	-	-	-	-	-	12	-	-	-	-	-	12	
24	-	-	-	-	-	9	-	-	-	-	9	-	-	-	-	-	-	9	-	-	-	-	-	9	
48	-	-	-	-	-	6	-	-	-	-	6	-	-	-	-	-	-	6	-	-	-	-	-	6	
72	-	-	-	-	-	3	-	-	-	-	3	-	-	-	-	-	-	3	-	-	-	-	-	3	
Total	-	-	-	-	-	11	-	-	-	-	11	-	-	-	-	-	-	12	-	-	-	-	-	12	
Subcutaneous																									
0	-	-	2	-	-	11	-	-	2	-	11	-	-	5	-	-	12	-	-	5	-	-	5	-	12
4	-	-	1	-	-	11	-	-	-	-	11	-	-	1	-	-	12	-	-	-	-	-	-	-	12
24	-	-	-	-	-	9	-	-	-	-	9	-	-	-	-	-	-	9	-	-	-	-	-	9	
48	-	-	-	-	-	6	-	-	-	-	6	-	-	-	-	-	-	6	-	-	-	-	-	6	
72	-	-	-	-	-	3	-	-	-	-	3	-	-	-	-	-	-	3	-	-	-	-	-	3	
Total	-	-	2	-	-	11	-	-	2	-	11	-	-	5	-	-	12	-	-	5	-	-	5	-	12

7.250000

7.250000 7.250000 7.250000 (log)

DISCUSSION

The clinical observations following the intravenous, intra-venous, intra-arterial, intramuscular, and subcutaneous injection of hypertonic saline/dextran, hypertonic saline, Dextran 70[®], and Ringer's lactate could all be attributed to the perivascular leakage of blood subsequent to needle insertion. Following intravenous injection of HS and DEX 70, bruising was observed at an increased incidence relative to injections of HSD or LRS. However, the majority of bruises had resolved by 72 hours in those animals observed through the 14-day study period. The increased incidence of signs at the intra-arterial sites was due to the greater arterial blood pressure relative to the pressure at other injection sites, which resulted in increased extravasation of blood following intra-arterial injections. The occurrence of blebs following subcutaneous and paravenous injections were considered normal sequelae to injection technique. None of the test solutions caused clinical signs following intramuscular injection.

The signs of muscle degeneration and associated inflammation observed grossly and microscopically at necropsy were not a consequence of either hemorrhage or the introduction of foreign material, i.e. fur, introduced as a result of needle insertion. The muscle degeneration and inflammation were considered to be of little clinical significance and were not expected to heal with no residual morphological or functional alteration.

The results of this study suggest that hypertonic saline/dextran and Dextran 70[®] are no more irritating than Ringer's lactate following intravenously injection.

CONCLUSION

The test compound, hypertonic saline/Dextran 70[®], and control solutions, hypertonic saline and Dextran 70[®], were no more irritating than Ringer's lactate under the conditions of this study.

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REFERENCES (cont.)

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	Page
Chemical Data.....	17
Animal Data.....	21
Historical List of events.....	22
Individual Animal Histories.....	24
Individual Body Weights.....	49
Pathology Report.....	51

Appendix A: CHEMICAL DATA



CERTIFICATE OF ANALYSIS 1988-12-19

6 % DEXTRAN 70 IN 7,5 %
SODIUM CHLORIDE INJECTION

Charge No. NC 54845

Inherent viscosity	27 ml/g
Absorbance (375 nm, 10 mm)	0,006
pH	4,6
Heavy metals	< 5 ppm
Sodium chloride	74,7 g/1000 ml
Dextran 70	60 g/1000 ml
Particulate matter	passed test
Sterility	passed test
Pyrogens	passed test

Released for clinical trials.

Pharmacia AB
Analytical Chemistry Department

Elisabet Fransson
Elisabet Fransson

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Pharmacia AB S-751 82 Uppsala Sweden	Nat 018-18 30 00 Int +46 18 18 30 00	pharmacia uppsala	76027 pharmup:s	Nat 018-15 41 35 Int +46 18 15 41 35

Appendix A (cont.): CHEMICAL DATA



CERTIFICATE OF ANALYSIS

7.5% SODIUM CHLORIDE

	Charged to
Identification	passed test
Absorbance	0.000
pH	6.0
Heavy metals	< 5 ppm
Sodium chloride	95.0 g/1000 ml
Particulate matter	passed test
Sterility	passed test
Pyrogens	passed test
Releasued for biological trials.	

Pharmacia AB
Analytical Chemistry Department

Elisabet Fransson
Elisabet Fransson

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Appendix A (cont.): CHEMICAL DATA



Pharmacia

Certificate of analysis

Name: MACRODEX 60 mg/ml in Normal saline

Item No.: 10-4510-00

Lot No.: NE 54941

Test		Result	Tolerance limit	Method
Inherent viscosity	ml/g	26	25 - 28	03700
Colour		0,01	Max. 0,04	03811
pH		4,9	4,0 - 7,0	USP XX p. 968
Heavy metals ppm		< 5	Max. 5	USP XX p. 909
Assay for				
- sodium chloride	g/1000ml	8,88	8,10 - 9,90	02355
- dextran 70	g/1000ml	59	54 - 66	02356
Sterility		Passed test	To pass test	02885
Pyrogens		Passed test	To pass test	02983

The identity is assured through strict adherence to established GMP rules throughout the manufacturing procedures.

Released for sale: 1987-05-25

Pharmacia AB
Quality Control Department

Mats Wiberg

M09

Pharmacia AB
S-751 82 UPPSALA
Sweden

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Nat 018 - 163000
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76027 pharmus

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Appendix A (cont.): CHEMICAL DATA



CERTIFICATE OF ANALYSIS 1989-12-19

LACTATED RINGER'S INJECTION

Charge No. NC 54847

pH	5,8
Heavy metals	< 5 ppm
Sodium	127 mmol/1000 ml
Potassium	3,91 mmol/1000 ml
Calcium	1,30 mmol/1000 ml
Chloride	105,5 mmol/1000 ml
Lactate	27,2 mmol/1000 ml
Particulate matter	passed test
Sterility	passed test
Pyrogens	passed test

Released for clinical trials.

Pharmacia AB
Analytical Chemistry Department

Elisabet Fransson
Elisabet Fransson

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Appendix B: ANIMAL DATA

Species: *Cryptotomus cuniculus*

Strain: New Zealand White

Supplier: Elkhorn Rabbitry
5265 Starr Way
Watsonville, CA 95076

Sex: Male

Date of birth: 21 Jan 88
23 Jan 88
1 Feb 88
5 Feb 88

Animal identification: Weight bias, stratified animal
identification (XYBICON Medical Systems PATH/TOX AESLCT Animal
identification program)

Animals in each group:	1a	2
	1b	3
	2a	3
	2b	3
	3a	3
	3a	3
	4a	3
	4b	3

Condition of animals at start of study: Normal

Average weight range at dosing: 2.4 - 3.9 kg

Identification procedures: Neck band

Period of acclimation: Quarantine/acclimation 21 April 1988
to 12 June 1988

Irritation: The laboratory rabbit is the standard
experimental model for local irritation studies and is accepted
by all regulatory agencies.

Appendix C: HISTORICAL LISTING OF STUDY EVENTS

<u>Date</u>	<u>Event</u>
21 Apr 88	Animals arrived at LAIR. They were observed for illness and caged in the GLP Suite. Twenty-six animals were assigned to the study.
22, 29 Apr, 6, 13, 20, 27 May, 3, 7 Jun 88	Animals were weighed.
22 Apr 88 - 9 Jun 88	Animals were observed twice daily.
2 May 88	Quality control animals were submitted for necropsy.
6 Jun 88	Animals were randomized into groups.
6 Jun 88	Animals were shaved.
7 Jun 88	Animals were dosed between 0900 and 1230 hours. Observations and inspection of injection sites were conducted immediately after dosing and four hours later. Group 1 animals were weighed and submitted for necropsy four hours after dosing was completed.
8 Jun 88	Animals were observed in a.m. and p.m. for clinical signs. Injection sites were inspected 24 hours after dosing was completed. Group 2 animals were weighed and submitted for necropsy 24 hours after dosing was completed.
9 Jun 88	Animals were observed in a.m. and p.m. for clinical signs. Injection sites were inspected 48 hours after dosing was completed. Group 3 animals were weighed and submitted for necropsy 48 hours after dosing was completed.

**Appendix C (cont.): HISTORICAL LISTING
OF STUDY EVENTS**

<u>Date</u>	<u>Event</u>
10 Jun 88	Animals were observed in a.m. and p.m. for clinical signs. Injection sites were inspected 72 hours after dosing was completed. Group 4 animals were weighed and submitted for necropsy 72 hours after dosing was completed.

Appendix D: INDIVIDUAL ANIMAL HISTORIES

Clinical Observation Severity Code

<u>Severity</u>	<u>Lesion Size (mm)</u>
1	≤ 3
2	4 - 6
3	7 - 9
4	10 - 12
5	> 12

Appendix D (cont.) : INDIVIDUAL ANIMAL HISTORIES

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INDIVIDUAL ANIMAL DATA DUMP TABLE
 STUDY NUMBER: 88004

STUDY START DATE: 07-JUN-88

ANIMAL: 88F00095

DAY OF DEATH: 1

STATUS: NORMAL, EUTHANIZED

TERMINAL BODY WEIGHT: 3.4 (KGS)

DATE	DAY/WEEK OF STUDY	TIME OF DAY	<< C L I N I C A L O B S E R V A T I O N S >		SEVERITY
			OBSERVATIONS AND COMMENTS		
07-JUN-88	1/1	11:07	RIGHT INTRA-ARTERIAL SITE / HEMATOMA	1	
07-JUN-88	1/1	13:06	RIGHT INTRA-ARTERIAL SITE / HEMATOMA	1	
			LEFT INTRA-ARTERIAL SITE / BRUISE	5	
				2	

Saucha et al--26

Appendix D (cont.): INDIVIDUAL ANIMAL HISTORIES

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INDIVIDUAL ANIMAL DATA DUMP TABLE
STUDY NUMBER: 88004
PRINTED: 23-NOV-88
PAGE: 2

STUDY START DATE: 07-JUN-88

ANIMAL: 88F00114 DAY OF DEATH: -2

STATUS: FOUND DEAD

TERMINAL BODY WEIGHT: ---

<< C L I N I C A L O B S E R V A T I O N S >
DATE DAY/WEEK OF STUDY TIME OF DAY OBSERVATIONS AND COMMENTS
05-JUN-88 -2/-1 08:00 NONE

APPENDIX D (cont.): INDIVIDUAL ANIMAL HISTORIES

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INDIVIDUAL ANIMAL DATA DUMP TABLE
 STUDY NUMBER: 88004

STUDY START DATE: 07-JUN-88

ANIMAL:	DAY OF DEATH:	DAY/WEEK OF STUDY	TIME OF DAY	C L I N I C A L O B S E R V A T I O N S	TERMINAL BODY WEIGHT:
88F00139	1	1/1	11:08	STATUS: NORMAL, EUTHANIZED	3.4 (KGS)
			13:12	LEFT INTRA-ARTERIAL SITE / HEMATOMA	
				LEFT INTRA-ARTERIAL SITE / HEMATOMA	

DATE	DAY/WEEK OF STUDY	TIME OF DAY	OBSERVATIONS AND COMMENTS	SEVERITY
07-JUN-88	1/1	11:08	LEFT INTRA-ARTERIAL SITE / HEMATOMA	2
07-JUN-88	1/1	13:12	LEFT INTRA-ARTERIAL SITE / HEMATOMA	1

Appendix D (cont.): INDIVIDUAL ANIMAL HISTORIES

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ANIMAL: 88000101

DAY OF DEATH: 1

STATUS: NORMAL, EUTHANIZED

DATE	DAY/WEEK OF STUDY	TIME OF DAY	<< CLINICAL OBSERVATIONS AND COMMENTS >>		SEVERITY
			OBSERVATIONS AND COMMENTS		
07-JUN-88	1/1	11:11	RIGHT INTRA-ARTERIAL SITE / HEMATOMA	1	
07-JUN-88	1/1	13:20	RIGHT INTRA-ARTERIAL SITE / HEMATOMA LEFT INTRA-ARTERIAL SITE / HEMATOMA	3	2

PRINTED: 23-NOV-88
 PAGE: 4

INDIVIDUAL ANIMAL DATA DUMP TABLE
 STUDY NUMBER: 88004

STUDY START DATE: 07-JUN-88

		TERMINAL BODY WEIGHT:	2.9 (KGS)

Appendix D (cont.): INDIVIDUAL ANIMAL HISTORIES

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INDIVIDUAL ANIMAL DATA DUMP TABLE
 STUDY NUMBER: 88004

STUDY START DATE: 07-JUN-88

ANIMAL:	DAY OF DEATH:	DAY/WEEK OF STUDY	TIME OF DAY	CLINICAL OBSERVATIONS AND COMMENTS	TERMINAL BODY WEIGHT:
88F00110	1			STATUS: NORMAL, EUTHANIZED	3.5 (KGS)
				<< CLINICAL OBSERVATIONS >>	
				OBSERVATIONS AND COMMENTS	
				SEVERITY	
07-JUN-88	1/1	1/1	11:14	LEFT INTRA-ARTERIAL SITE / HEMATOMA	1
07-JUN-88	1/1	1/1	14:03	RIGHT INTRA-ARTERIAL SITE / HEMATOMA	2
				LEFT INTRAVENOUS SITE / HEMATOMA	1
				LEFT INTRA-ARTERIAL SITE / HEMATOMA	2

Appendix D (cont.): INDIVIDUAL ANIMAL HISTORIES

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STUDY START DATE: 07-JUN-88

ANIMAL: 88F00108 DAY OF DEATH: 1 STATUS: NORMAL, EUTHANIZED

DATE	DAY/WEEK OF STUDY	TIME OF DAY	<< CLINICAL OBSERVATIONS AND COMMENTS >>		SEVERITY
			OBSERVATIONS AND COMMENTS		
07-JUN-88	1/1	11:30	LEFT SUBCUTANEOUS SITE / SUBCUTANEOUS BLEB	4	
			RIGHT PARAVENOUS SITE / SUBCUTANEOUS BLEB	1	
			RIGHT INTRA-ARTERIAL SITE / HEMATOMA	3	
			RIGHT SUBCUTANEOUS SITE / SUBCUTANEOUS BLEB	4	
			LEFT PARAVENOUS SITE / SUBCUTANEOUS BLEB	1	
			RIGHT INTRA-ARTERIAL SITE / HEMATOMA	4	
			LEFT INTRAVENOUS SITE / HEMATOMA	1	
			LEFT INTRA-ARTERIAL SITE / HEMATOMA	1	

Appendix D (cont.): INDIVIDUAL ANIMAL HISTORIES

LETTERMAN ARMY INSTITUTE OF RESEARCH
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INDIVIDUAL ANIMAL DATA DUMP TABLE
 STUDY NUMBER: 88004

STUDY START DATE: 07-JUN-88

ANIMAL: 88F00107

DAY OF DEATH:

2

STATUS: NORMAL, EUTHANIZED

DATE	DAY/WEEK OF STUDY	TIME OF DAY	<< C L I N I C A L O B S E R V A T I O N S >>		SEVERITY
			OBSERVATIONS AND COMMENTS		
07-JUN-88	1/1	11:33	LEFT INTRA-ARTERIAL SITE / HEMATOMA	1	
07-JUN-88	1/1	14:30	RIGHT INTRA-ARTERIAL SITE / BRUISE	2	
08-JUN-88	2/1	10:37	LEFT INTRA-ARTERIAL SITE / HEMATOMA	1	
			RIGHT INTRAVENOUS SITE / BRUISE	1	
			LEFT INTRA-ARTERIAL SITE / HEMATOMA	2	

Appendix D (cont.) : INDIVIDUAL ANIMAL HISTORIES

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STUDY START DATE: 07-JUN-88

ANIMAL: 88F00104 DAY OF DEATH: 2 STATUS: NORMAL, EUTHANIZED

DATE	DAY/WEEK OF STUDY	TIME OF DAY	<< C L I N I C A L O B S E R V A T I O N S >		SEVERITY
			OBSERVATIONS AND COMMENTS	CLINICAL OBSERVATIONS	
07-JUN-88	1/1	11:36	LEFT SUBCUTANEOUS SITE / SUBCUTANEOUS BLEB		3
			RIGHT INTRA-ARTERIAL SITE / HEMATOMA		2
07-JUN-88	1/1	14:31	RIGHT SUBCUTANEOUS SITE / SUBCUTANEOUS BLEB		4
			RIGHT INTRA-ARTERIAL SITE / HEMATOMA		3
			RIGHT SUBCUTANEOUS SITE / SUBCUTANEOUS BLEB		3
08-JUN-88	2/1	12:48	LEFT INTRA-ARTERIAL SITE / HEMATOMA		3
			RIGHT INTRA-ARTERIAL SITE / BRUISE		5
			LEFT INTRA-ARTERIAL SITE / BRUISE		3

Appendix D (cont.): INDIVIDUAL ANIMAL HISTORIES

LETTERMAN ARMY INSTITUTE OF RESEARCH
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INDIVIDUAL ANIMAL DATA DUMP TABLE
 STUDY NUMBER: 88004

STUDY START DATE: 07-JUN-88

ANIMAL:	DAY OF DEATH:	DAY/WEEK OF STUDY	TIME OF DAY	CLINICAL OBSERVATIONS AND COMMENTS	TERMINAL BODY WEIGHT:
88F00100	2			STATUS: NORMAL, EUTHANIZED	3.7 (KGS)
		<<		C L I N I C A L O B S E R V A T I O N S >	
				O B S E R V A T I O N S	
				SEVERITY	
07-JUN-88	1/1	11:39		LEFT SUBCUTANEOUS SITE / SUBCUTANEOUS BLEB	3
				RIGHT INTRA-ARTERIAL SITE / HEMATOMA	2
				RIGHT SUBCUTANEOUS SITE / SUBCUTANEOUS BLEB	3
				LEFT INTRA-ARTERIAL SITE / HEMATOMA	3
07-JUN-88	1/1	14:32		RIGHT INTRA-ARTERIAL SITE / HEMATOMA	5
				LEFT INTRA-ARTERIAL SITE / HEMATOMA	4
08-JUN-88	2/1	10:33		RIGHT INTRA-ARTERIAL SITE / BRUISE	5
				LEFT INTRA-ARTERIAL SITE / BRUISE	4

Appendix D (cont.): INDIVIDUAL ANIMAL HISTORIES

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INDIVIDUAL ANIMAL DATA DUMP TABLE
 STUDY NUMBER: 88004
 STUDY START DATE: 07-JUN-88

ANIMAL: 88F00111 DAY OF DEATH: 2

DATE	DAY/WEEK OF STUDY	TIME OF DAY	<< CLINICAL OBSERVATIONS AND COMMENTS >>	TERMINAL BODY WEIGHT: 3.4 (KGS)
07-JUN-88	1/1	11:42	NORMAL / NO SIGNIFICANT FINDINGS	
07-JUN-88	1/1	14:47	RIGHT INTRAVENOUS SITE / BRUISE	1
08-JUN-88	2/1	10:45	LEFT INTRAVENOUS SITE / BRUISE	1
			RIGHT INTRAVENOUS SITE / BRUISE	1
			LEFT INTRAVENOUS SITE / BRUISE	1
			LEFT INTRA-ARTERIAL SITE / BRUISE	1

Appendix D (cont.): INDIVIDUAL ANIMAL HISTORIES

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INDIVIDUAL ANIMAL DATA DUMP TABLE
 STUDY NUMBER: 88004

PRINTED: 23-NOV-88
 PAGE: 11

STUDY START DATE: 07-JUN-88

ANIMAL:	DAY OF DEATH:	DAY / WEEK OF STUDY	TIME OF DAY	<< C L I N I C A L O B S E R V A T I O N S >	TERMINAL BODY WEIGHT:	SEVERITY
				O B S E R V A T I O N S AND COMMENTS		
88F00093	2			STATUS: NORMAL, EUTHANIZED	3.2 (KGS)	
07 - JUN - 88		1/1	11:45	LEFT SUBCUTANEOUS SITE / SUBCUTANEOUS BLEB RIGHT INTRAVENOUS SITE / HEMATOMA RIGHT INTRA-ARTERIAL SITE / HEMATOMA RIGHT SUBCUTANEOUS SITE / SUBCUTANEOUS BLEB LEFT INTRA-ARTERIAL SITE / HEMATOMA RIGHT INTRAVENOUS SITE / HEMATOMA RIGHT INTRA-ARTERIAL SITE / HEMATOMA LEFT INTRA-ARTERIAL SITE / HEMATOMA RIGHT SUBCUTANEOUS SITE / SUBCUTANEOUS BLEB LEFT INTRA-ARTERIAL SITE / HEMATOMA RIGHT INTRAVENOUS SITE / BRUISE RIGHT INTRA-ARTERIAL SITE / BRUISE LEFT INTRA-ARTERIAL SITE / BRUISE	2 1 1 1 2 1 1 1 2 1 1 1 2 1	
07 - JUN - 88		1/1	14:49			
08 - JUN - 88		2/1	10:47			

Appendix D (cont.): INDIVIDUAL ANIMAL HISTORIES

LETTERMAN ARMY INSTITUTE OF RESEARCH
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INDIVIDUAL ANIMAL DATA DUMP TABLE
 STUDY NUMBER: 88004

PRINTED: 23-NOV-88
 PAGE: 12

STUDY START DATE: 07-JUN-88

ANIMAL: 88F0094 DAY OF DEATH: 2 STATUS: NORMAL, EUTHANIZED

DATE	DAY/WEEK OF STUDY	TIME OF DAY	CLINICAL OBSERVATIONS AND COMMENTS	TERMINAL BODY WEIGHT: 3.1 (KGS)
07-JUN-88	1/1	11:47	RIGHT INTRA-ARTERIAL SITE / HEMATOMA LEFT PARAVENOUS SITE / SUBCUTANEOUS BLEB LEFT INTRA-ARTERIAL SITE / HEMATOMA RIGHT INTRAVENOUS SITE / BRUISE	2
07-JUN-88	1/1	14:50	RIGHT INTRA-ARTERIAL SITE / BRUISE LEFT INTRA-ARTERIAL SITE / HEMATOMA RIGHT INTRAVENOUS SITE / BRUISE	1
08-JUN-88	2/1	10:49	RIGHT INTRA-ARTERIAL SITE / HEMATOMA RIGHT INTRAVENOUS SITE / BRUISE LEFT INTRA-ARTERIAL SITE / BRUISE	2
				1

Appendix D (cont.) : INDIVIDUAL ANIMAL HISTORIES

LETTERMAN ARMY INSTITUTE OF RESEARCH
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INDIVIDUAL ANIMAL DATA DUMP TABLE
 STUDY NUMBER: 88004
 PAGE: 13

STUDY START DATE: 07-JUN-88

ANIMAL: 88F00092 DAY OF DEATH: 3

STATUS: NORMAL, EUTHANIZED

<< C L I N I C A L O B S E R V A T I O N S >				TERMINAL BODY WEIGHT: 3.4 (KGS)
DATE	DAY/WEEK OF STUDY	TIME OF DAY	OBSERVATIONS AND COMMENTS	SEVERITY
07-JUN-88	1/1	12:45	RIGHT INTRA-ARTERIAL SITE / HEMATOMA	1
07-JUN-88	1/1	16:31	LEFT INTRA-ARTERIAL SITE / HEMATOMA	1
08-JUN-88	2/1	10:53	RIGHT INTRA-ARTERIAL SITE / BRUISE	5
09-JUN-88	3/1	12:24	LEFT INTRA-ARTERIAL SITE / BRUISE	5
			RIGHT INTRA-ARTERIAL SITE / BRUISE	5
			LEFT INTRA-ARTERIAL SITE / HEMATOMA / BRUISE	4

Appendix D (cont.): INDIVIDUAL ANIMAL HISTORIES

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ANIMAL: 88F00105

DAY OF DEATH: 3

PRINTED: 23-NOV-88

PAGE: 14

INDIVIDUAL ANIMAL DATA DUMP TABLE

STUDY NUMBER: 88004

STUDY START DATE: 07-JUN-88

DATE	DAY/WEEK OF STUDY	TIME OF DAY	<< C L I N I C A L O B S E R V A T I O N S >>	TERMINAL BODY WEIGHT: 3.8 (KGS)
			CLINICAL OBSERVATIONS AND COMMENTS	SEVERITY
07-JUN-88	1/1	12:46	RIGHT INTRA-ARTERIAL SITE / HEMATOMA LEFT INTRA-ARTERIAL SITE / HEMATOMA	1
07-JUN-88	1/1	16:32	RIGHT INTRA-ARTERIAL SITE / BRUISE LEFT INTRA-ARTERIAL SITE / BRUISE	5
08-JUN-88	2/1	10:53	RIGHT INTRA-ARTERIAL SITE / BRUISE LEFT INTRA-ARTERIAL SITE / BRUISE	5
09-JUN-88	3/1	12:27	RIGHT INTRAVENOUS SITE / BRUISE RIGHT INTRA-ARTERIAL SITE / BRUISE LEFT INTRAVENOUS SITE / BRUISE	3 2 1
			LEFT INTRA-ARTERIAL SITE / BRUISE	2 1 5

Appendix D (cont.): INDIVIDUAL ANIMAL HISTORIES

LETTERMAN ARMY INSTITUTE OF RESEARCH
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INDIVIDUAL ANIMAL DATA DUMP TABLET
 STUDY NUMBER: 88004

STUDY START DATE: 07 JUN 88

ANIMAL:	DAY OF DEATH:	DAY	TIME OF DAY	C L I N I C A L O B S E R V A T I O N :	TERMINAL BODY WEIGHT:
<< C L I N I C A L O B S E R V A T I O N : >>					
DATE	DAY/WEEK OF STUDY	TIME OF DAY		OBSERVATIONS AND COMMENTS	SEVERITY
07 - JUN - 88	1 / 1	12:47		RIGHT INTRA-ARTERIAL SITE / HEMATOMA	1
07 - JUN - 88	1 / 1	16:36		LEFT INTRA-ARTERIAL SITE / HEMATOMA	1
				RIGHT INTRA-ARTERIAL SITE / BRUISE	2
				LEFT INTRA-ARTERIAL SITE / BRUISE	2
08 - JUN - 88	2 / 1	10:53		RIGHT INTRA-ARTERIAL SITE / BRUISE	2
				LEFT INTRA-ARTERIAL SITE / BRUISE	2
09 - JUN - 88	3 / 1	12:28		RIGHT INTRA-ARTERIAL SITE / BRUISE	1
				LEFT INTRAVENOUS SITE / BRUISE	2
				LEFT INTRA-ARTERIAL SITE / BRUISE	1

Appendix D (cont.): INDIVIDUAL ANIMAL HISTORIES

LETERMAN ARMY INSTITUTE OF RESEARCH
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 RABBIT/NEW ZEALAND WHITE

INDIVIDUAL ANIMAL DATA DUMP TABLE
 STUDY NUMBER: 88004
 PRINTED: 23-NOV-88
 PAGE: 16

STUDY START DATE: 07-JUN-88

ANIMAL:	DAY OF DEATH:	DAY	TIME OF DAY	<< CLINICAL OBSERVATIONS AND COMMENTS >>	TERMINAL BODY WEIGHT:	(KGS)
DATE	DAY/WEEK OF STUDY			OBSERVATIONS		SEVERITY
07-JUN-88	1/1		12:54	RIGHT INTRA-ARTERIAL SITE / HEMATOMA LEFT INTRA-ARTERIAL SITE / HEMATOMA	2	
07-JUN-88	1/1		16:38	RIGHT INTRA-ARTERIAL SITE / BRUISE LEFT INTRA-ARTERIAL SITE / BRUISE	1	
08-JUN-88	2/1		11:09	RIGHT INTRAVENOUS SITE / BRUISE RIGHT INTRA-ARTERIAL SITE / BRUISE LEFT INTRAVENOUS SITE / BRUISE	5	
09-JUN-88	3/1		12:36	LEFT INTRA-ARTERIAL SITE / BRUISE RIGHT INTRAVENOUS SITE / BRUISE RIGHT INTRA-ARTERIAL SITE / BRUISE LEFT INTRAVENOUS SITE / BRUISE LEFT INTRA-ARTERIAL SITE / BRUISE	4	
					3	
					5	
					1	
					2	
					2	
					1	
					2	

Appendix D (cont.): INDIVIDUAL ANIMAL HISTORIES

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INDIVIDUAL ANIMAL DATA DUMP TABLE
 STUDY NUMBER: 88004

PRINTED: 23 NOV-88
 PAGE: 17

STUDY START DATE: 07-JUN-88

ANIMAL: 88F00099

DAY OF DEATH:

3

STATUS: NORMAL, EUTHANIZED

DATE	DAY/WEEK OF STUDY	TIME OF DAY	<< CLINICAL OBSERVATIONS AND COMMENTS >	TERMINAL BODY WEIGHT:	3.5 (KGS)
DATE	DAY/WEEK OF STUDY	TIME OF DAY	OBSERVATIONS AND COMMENTS	SEVERITY	
07-JUN-88	1/1	12:56	LEFT SUBCUTANEOUS SITE / SUBCUTANEOUS BLEB	3	
			RIGHT INTRA-ARTERIAL SITE / HEMATOMA	1	
			RIGHT SUBCUTANEOUS SITE / SUBCUTANEOUS BLEB	2	
			LEFT INTRA-ARTERIAL SITE / HEMATOMA	1	
07-JUN-88	1/1	16:39	RIGHT INTRA-ARTERIAL SITE / BRUISE	5	
08-JUN-88	2/1	11:05	LEFT INTRA-ARTERIAL SITE / BRUISE	5	
			RIGHT INTRA-ARTERIAL SITE / BRUISE	3	
			LEFT INTRAVENOUS SITE / BRUISE	1	
			LEFT INTRA-ARTERIAL SITE / BRUISE	4	
09-JUN-88	3/1	12:32	RIGHT INTRAVENOUS SITE / BRUISE	1	
			RIGHT INTRA-ARTERIAL SITE / BRUISE	4	
			LEFT INTRAVENOUS SITE / BRUISE	1	
			LEFT INTRA-ARTERIAL SITE / BRUISE	3	

Appendix D (cont.): INDIVIDUAL ANIMAL HISTORIES

LETTERMAN ARMY INSTITUTE OF RESEARCH
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INDIVIDUAL ANIMAL DATA DUMP TABLE

STUDY NUMBER: 88004

STUDY START DATE: 07-JUN-88

ANIMAL: 88F00115

DAY OF DEATH:

3

STATUS: NORMAL, EUTHANIZED

DATE	DAY/WEEK OF STUDY	TIME OF DAY	<< C L I N I C A L O B S E R V A T I O N S >		TERMINAL BODY WEIGHT: 3.1 (KGS)
			OBSERVATIONS AND COMMENTS	SEVERITY	
07-JUN-88	1/1	12:57	RIGHT INTRA-ARTERIAL SITE / HEMATOMA	1	
07-JUN-88	1/1	16:48	RIGHT INTRA-ARTERIAL SITE / BRUISE	5	
			LEFT INTRA-ARTERIAL SITE / BRUISE	5	
08-JUN-88	2/1	11:06	RIGHT INTRA-ARTERIAL SITE / BRUISE	3	
			LEFT INTRA-ARTERIAL SITE / BRUISE	3	
09-JUN-88	3/1	12:33	RIGHT INTRA-ARTERIAL SITE / BRUISE	4	
			LEFT INTRA-ARTERIAL SITE / BRUISE	5	

PRINTED: 23-NOV-88
 PAGE: 18

Appendix D (cont.): INDIVIDUAL ANIMAL HISTORIES

LETTERMAN ARMY INSTITUTE OF RESEARCH
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 PRESIDIO OF SAN FRANCISCO, CA 94129
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INDIVIDUAL ANIMAL DATA DUMP TABLE
 STUDY NUMBER: 88004

STUDY START DATE: 07-JUN-88

ANIMAL:	DAY OF DEATH:	DAY	STATUS:	TERMINAL BODY WEIGHT:
DATE	DAY/WEEK OF STUDY	TIME OF DAY	<< CLINICAL OBSERVATIONS >>	3.7 (KGS)
			OBSERVATIONS AND COMMENTS	SEVERITY
07 - JUN - 88	1/1	12:48	RIGHT INTRA-ARTERIAL SITE / HEMATOMA LEFT PARAVENOUS SITE / SUBCUTANEOUS BLEB	1
07 - JUN - 88	1/1	16:58	LEFT INTRA-ARTERIAL SITE / HEMATOMA	1
08 - JUN - 88	2/1	10:54	RIGHT INTRA-ARTERIAL SITE / BRUISE LEFT INTRA-ARTERIAL SITE / BRUISE	1
09 - JUN - 88	3/1	12:29	RIGHT INTRA-ARTERIAL SITE / BRUISE LEFT INTRAVENOUS SITE / BRUISE	3
10 - JUN - 88	4/1	13:42	RIGHT INTRA-ARTERIAL SITE / NODULE LEFT INTRA-ARTERIAL SITE / NODULE	2

Zaucha et al - 44

Appendix D (cont.): INDIVIDUAL ANIMAL HISTORIES

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ANIMAL: 88F00096 DAY OF DEATH: 4 STUDY START DATE: 07 JUN 88
INDIVIDUAL ANIMAL DATA DUMP TABLE
STUDY NUMBER: 88004

PRINTED: 23-NOV-88
PAGE: 20

DATE	DAY/WEEK OF STUDY	TIME OF DAY	CLINICAL OBSERVATIONS AND COMMENTS	TERMINAL BODY WEIGHT:	SEVERITY
07-JUN-88	1/1	12:49	RIGHT PARAVENOUS SITE / SUBCUTANEOUS BLEB		
07-JUN-88	1/1	17:00	RIGHT INTRA-ARTERIAL SITE / HEMATOMA	1	
08-JUN-88	2/1	10:59	RIGHT INTRA-ARTERIAL SITE / BRUISE	1	
09-JUN-88	3/1	12:29	LEFT INTRA-ARTERIAL SITE / ERYTHEMA	4	
10-JUN-88	4/1	13:45	LEFT INTRA-ARTERIAL SITE / ERYTHEMA	1	
			NONE	2.6 (KGS)	

APPENDIX D (cont.): INDIVIDUAL ANIMAL HISTORIES

LETTERMAN ARMY INSTITUTE OF RESEARCH
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INDIVIDUAL ANIMAL DATA DUMP TABLE
 STUDY NUMBER: 88004

STUDY START DATE: 07-JUN-88

ANIMAL: 88F00106 DAY OF DEATH: 4

STATUS: NORMAL, EUTHANIZED

DATE	DAY/WEEK OF STUDY	TIME OF DAY	<< C L I N I C A L O B S E R V A T I O N S >		TERMINAL BODY WEIGHT: 4.0 (KGS)	SEVERITY
			COMMENTS	OBSERVATIONS AND COMMENTS		
07-JUN-88	1/1	12:49	RIGHT INTRA-ARTERIAL SITE / HEMATOMA	LEFT INTRA-ARTERIAL SITE / HEMATOMA		1
07-JUN-88	1/1	17:01	RIGHT PARAVENOUS SITE / BRUISE	RIGHT INTRA-ARTERIAL SITE / BRUISE		5
08-JUN-88	2/1	11:00	LEFT INTRA-ARTERIAL SITE / BRUISE	RIGHT PARAVENOUS SITE / BRUISE		4
09-JUN-88	3/1	12:30	RIGHT INTRA-ARTERIAL SITE / BRUISE	LEFT INTRA-ARTERIAL SITE / BRUISE		5
10-JUN-88	4/1	13:49	RIGHT PARAVENOUS SITE / BRUISE	RIGHT INTRA-ARTERIAL SITE / HEMATOMA		1
10-JUN-88	4/1	14:00	NONE	/ BRUISE		1

Appendix D (cont.): INDIVIDUAL ANIMAL HISTORIES

LETTERMAN ARMY INSTITUTE OF RESEARCH
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INDIVIDUAL ANIMAL DATA DUMP TABLE
 STUDY NUMBER: 88004
 STUDY START DATE: 07-JUN-88

PRINTED: 23-NOV-88
 PAGE: 22

ANIMAL: 88F00103 DAY OF DEATH: 4 STATUS: NORMAL, EUTHANIZED

DATE	DAY/WEEK OF STUDY	TIME OF DAY	<< CLINICAL OBSERVATIONS AND COMMENTS >>		SEVERITY
			OBSERVATIONS	COMMENTS	
07-JUN-88	1/1	12:58	RIGHT INTRA-ARTERIAL SITE / HEMATOMA		1
07-JUN-88	1/1	16:52	LEFT INTRA-ARTERIAL SITE / HEMATOMA		1
08-JUN-88	2/1	11:06	RIGHT INTRAVENOUS SITE / BRUISE		1
08-JUN-88	2/1	11:06	RIGHT INTRA-ARTERIAL SITE / BRUISE		3
08-JUN-88	2/1	11:06	LEFT INTRA-ARTERIAL SITE / BRUISE		4
08-JUN-88	2/1	11:06	RIGHT INTRAVENOUS SITE / BRUISE		1
08-JUN-88	2/1	11:06	RIGHT INTRA-ARTERIAL SITE / BRUISE		5
09-JUN-88	3/1	12:34	LEFT INTRA-ARTERIAL SITE / BRUISE		4
10-JUN-88	4/1	14:08	RIGHT INTRA-ARTERIAL SITE / NODULE		5
			LEFT INTRA-ARTERIAL SITE / BRUISE		5

APPENDIX D (cont.): INDIVIDUAL ANIMAL HISTORIES

LETTERRMAN ARMY INSTITUTE OF RESEARCH
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 RABBIT/NEW ZEALAND WHITE

INDIVIDUAL ANIMAL DATA DUMP TABLE
 STUDY NUMBER: 88004

STUDY START DATE: 07-JUN-88

ANIMAL: 88F00116 DAY OF DEATH:

4 STATUS: NORMAL, EUTHANIZED

DATE	DAY/WEEK OF STUDY	TIME OF DAY	OBSERVATIONS AND COMMENTS	C L I N I C A L O B S E R V A T I O N S	TERMINAL BODY WEIGHT: 3.6 (KGS)	SEVERITY
07-JUN-88	1/1	12:59	LEFT SUBCUTANEOUS SITE / SUBCUTANEOUS BLEB			2
07-JUN-88	1/1	16:53	RIGHT SUBCUTANEOUS SITE / SUBCUTANEOUS BLEB			2
08-JUN-88	2/1	11:07	RIGHT INTRA-ARTERIAL SITE / BRUISE			5
08-JUN-88	2/1	12:34	LEFT INTRA-ARTERIAL SITE / BRUISE			4
09-JUN-88	3/1		RIGHT INTRAVENOUS SITE / BRUISE			5
09-JUN-88	3/1		RIGHT PARAVENOUS SITE / BRUISE			5
09-JUN-88	3/1		RIGHT INTRA-ARTERIAL SITE / BRUISE			4
10-JUN-88	4/1	14:10	LEFT INTRAVENOUS SITE / BRUISE			1
10-JUN-88	4/1		LEFT INTRA-ARTERIAL SITE / BRUISE			5
10-JUN-88	4/1		RIGHT INTRAVENOUS SITE / BRUISE			5
10-JUN-88	4/1		RIGHT PARAVENOUS SITE / BRUISE			5
10-JUN-88	4/1		RIGHT INTRA-ARTERIAL SITE / BRUISE			4
			LEFT INTRA-ARTERIAL SITE / BRUISE			5

Appendix D (cont.): INDIVIDUAL ANIMAL HISTORIES

LETTERMAN ARMY INSTITUTE OF RESEARCH
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 RABBIT/NEW ZEALAND WHITE

INDIVIDUAL ANIMAL DATA DUMP TABLE
 STUDY NUMBER: 88004
 STUDY START DATE: 07-JUN-88

DATE	DAY/WEEK OF STUDY	TIME OF DAY	<< CLINICAL OBSERVATIONS AND COMMENTS >>		SEVERITY
			STUDY	OBSERVATIONS AND COMMENTS	
07-JUN-88	1/1	13:00		LEFT SUBCUTANEOUS SITE / SUBCUTANEOUS BLEB RIGHT PARAVENOUS SITE / SUBCUTANEOUS BLEB	2
				RIGHT INTRA-ARTERIAL SITE / HEMATOMA	2
07-JUN-88	1/1	16:55		RIGHT SUBCUTANEOUS SITE / SUBCUTANEOUS BLEB	1
				RIGHT PARAVENOUS SITE / BRUISE	2
08-JUN-88	2/1	11:08		RIGHT INTRA-ARTERIAL SITE / BRUISE	1
				LEFT INTRA-ARTERIAL SITE / BRUISE	4
				RIGHT PARAVENOUS SITE / BRUISE	2
				RIGHT INTRA-ARTERIAL SITE / BRUISE	1
				LEFT INTRAVENOUS SITE / BRUISE	5
				LEFT PARAVENOUS SITE / BRUISE	1
09-JUN-88	3/1	12:35		LEFT INTRA-ARTERIAL SITE / BRUISE	1
				RIGHT PARAVENOUS SITE / BRUISE	1
				RIGHT INTRA-ARTERIAL SITE / BRUISE	4
10-JUN-88	4/1	14:06		LEFT INTRA-ARTERIAL SITE / BRUISE	5
				NONE	

Appendix E: BODY WEIGHTS (KG)

Animal	Group/ Subgroup	-46	-39	-32	-25	Day of Study -18	-11	-4	Day of Study			
									-18	-11	-4	
88F00095	1/a	2.48	2.69	2.74	3.06	2.95	3.14	3.29	3.38			
88F00114	1/a	2.45	2.64	2.50	2.30	2.55	2.64	2.81				
88F00109	1/a	2.52	2.61	2.63	2.88	3.09	3.21	3.45	3.59			
Mean		2.48	2.65	2.62	2.75	2.86	3.06	3.18	3.39			
Std Dev		0.03	0.04	0.12	0.39	0.28	0.20	0.33	0.01			
SEM		0.02	0.02	0.07	0.23	0.16	0.11	0.19	0.01			
88F00107	2/a	2.48	2.63	2.77	3.16	3.23	3.50	3.62	3.67	3.65		
88F00104	2/a	2.10	2.50	2.54	2.75	2.96	3.16	3.27	3.29	3.36		
88F00100	2/a	2.53	2.85	2.77	3.06	3.16	3.46	3.67	3.63	3.71		
Mean		2.37	2.66	2.69	2.99	3.12	3.37	3.52	3.53	3.57		
Std Dev		0.24	0.18	0.13	0.21	0.14	0.19	0.22	0.21	0.19		
SEM		0.14	0.10	0.08	0.12	0.08	0.11	0.13	0.12	0.11		
88F00092	3/a	2.35	2.63	2.80	3.00	2.92	3.13	3.27	3.33	3.36		
88F00105	3/a	2.26	2.45	2.58	2.98	3.11	3.53	3.62	3.68	3.76		
88F00112	3/a	2.28	2.35	2.53	2.68	2.70	2.91	3.13	3.11	3.06		
Mean		2.30	2.47	2.64	2.89	2.91	3.19	3.34	3.37	3.39		
Std Dev		0.05	0.14	0.14	0.18	0.21	0.31	0.25	0.29	0.35		
SEM		0.03	0.08	0.08	0.10	0.12	0.18	0.15	0.17	0.20		
88F00091	4/a	2.30	2.50	2.70	2.88	3.07	3.39	3.40	3.60	3.66		
88F00096	4/a	2.55	2.63	2.73	2.85	2.21	2.08	2.29	2.40	2.59		
88F00106	4/a	2.46	2.78	2.86	3.21	3.39	3.67	3.84	3.89	3.99		
Mean		2.44	2.64	2.76	2.98	2.89	3.05	3.18	3.20	3.41		
Std Dev		0.13	0.14	0.08	0.20	0.61	0.85	0.80	0.79	0.73		
SEM		0.07	0.08	0.05	0.12	0.35	0.49	0.46	0.42	0.42		

Appendix E (cont.) : BODY WEIGHTS (KG)

Animal	Group/ Subgroup	-46	-39	-32	Day of Study				BODY WEIGHTS (KG)
					-25	-18	-11	-4	
88F00101	1/b	2.29	2.54	2.62	2.82	2.70	2.92	3.07	2.89
88F00110	1/b	2.18	2.53	2.73	2.96	3.13	3.34	3.46	3.45
88F00108	1/b	2.34	2.71	2.90	3.19	3.32	3.60	3.77	3.59
Mean		2.27	2.59	2.75	2.99	3.05	3.29	3.43	3.31
Std Dev		0.08	0.10	0.14	0.19	0.32	0.34	0.35	0.37
SEM		0.05	0.06	0.08	0.11	0.18	0.20	0.20	0.21
88F00111	2/b	2.28	2.65	2.79	2.80	3.00	3.24	3.40	3.38
88F00093	2/b	2.15	2.41	2.36	2.52	2.73	2.92	3.11	3.16
88F00094	2/b	2.30	2.16	2.53	2.78	2.38	2.62	2.88	3.05
Mean		2.24	2.41	2.56	2.70	2.70	2.93	3.13	3.23
Std Dev		0.08	0.25	0.22	0.16	0.31	0.31	0.26	0.15
SEM		0.05	0.14	0.12	0.09	0.18	0.18	0.15	0.10
88F00102	3/b	2.20	2.48	2.61	2.92	2.99	3.31	3.34	3.46
88F00099	3/b	2.44	2.70	2.72	3.01	3.17	3.34	3.38	3.46
88F00115	3/b	2.25	2.48	2.44	2.84	2.77	3.04	3.12	3.25
Mean		2.30	2.55	2.59	2.92	2.98	3.23	3.28	3.39
Std Dev		0.12	0.13	0.14	0.08	0.20	0.16	0.14	0.12
SEM		0.07	0.07	0.08	0.05	0.12	0.10	0.08	0.07
88F00103	4/b	2.02	2.35	2.48	2.68	2.88	3.08	3.14	3.26
88F00116	4/b	2.60	2.74	2.79	2.64	2.92	3.20	3.34	3.49
88F00098	4/b	2.52	2.75	2.66	2.93	2.87	3.26	3.19	3.21
Mean		2.38	2.61	2.71	2.75	2.89	3.11	3.22	3.34
Std Dev		0.32	0.23	0.20	0.16	0.03	0.08	0.10	0.15
SEM		0.15	0.12	0.12	0.09	0.02	0.04	0.04	0.10

Appendix F: PATHOLOGY REPORT

GLP STUDY 88004

Principal Investigator: CPT Gary Zaucha
Co-Principal Investigator: CPT Denzil Frost
Pathologist: MAJ David Young

I. INTRODUCTION

Study: Local Irritation Study
Test Compound: Hypertonic Saline/Dextran Solution (HSD)
Animal: Rabbit, New Zealand White, 2.5-3.5 kg, Male.

Usage Groups:

Group 1 (controls)	Lactated Ringers Solution
Group 2	Hypertonic Saline/Dextran Solution
Group 3	Hypertonic Saline
Group 4	Dextran 70®

II. SUMMARY OF PROCEDURES:

Euthanasia: Ketamine, IM followed by Sodium Pentobarbital, IC

Fixative: 10% Neutral Buffered Formalin

Histopathology: Routine

Other Procedures: Gross observation and measurement of injection sites.

III. GROSS FINDINGS: Measurements of the injection sites were made at necropsy. The sites were scored on the area (in mm²) of observable/palpable skin blebbing or displacement. The grading criteria are as listed in Table 1. The incidence summary of all gross findings is listed in Table 2.

IV. MICROSCOPIC FINDINGS: Tissues saved for microscopic evaluation from all groups were skin sections from the 5 injection sites and muscle from site 5 (thigh) which exhibited gross changes. Three sections of skin from each subject on site was taken; one from the actual site of injection and sections 1 cm distal and 1 cm proximal to the injection sites. All 3 sections per site were evaluated and the rating was based on the most severely affected section.

Table 3 lists the incidence summary (with percentages) of microscopic observation for all animals. Table 4 contains the incidence summary of non-neoplastic graded microscopic diagnoses evaluated using the Kolmogorov-Smirnov

Appendix F (cont.): PATHOLOGY REPORT

two-tailed test. This analysis revealed no significant difference from controls at the 0.05 level. Annex A lists the body weight, gross findings and microscopic diagnoses for each individual animal in all groups.

The most common lesion noted in both control and experimental groups was hemorrhage, frequently with an associated acute to subacute dermatitis. Minimal to mild skeletal muscle degeneration was occasionally present, primarily in the thoracic and thigh injection sites, with an infrequent minimal acute myositis. The inflammation, and to a lesser degree, the muscle degenerative changes appear to be a consequence of the hemorrhage or from foreign material (i.e., fur) in the dermis as a result of the injection. All hemorrhage and associated inflammation were likely to resolve without permanent morphologic or functional alteration.

V. SUMMARY COMMENTS: Dermal and subcutaneous hemorrhage occurred frequently without significant differences in all groups. Acute to subacute inflammation, occurring with less frequency, was also present in all groups and was a direct and expected response to hemorrhage. Moderate acute inflammation was almost always associated with fragments of fur displaced within the dermis. Although not evident from the appendices, subjectively the acute inflammatory responses were predominantly seen in the 4 and 24 hour interim sacrifice animals and the subacute inflammation was primarily in the older lesions (48 and 72 hours). Skeletal muscle degeneration, sporadically found in all groups, may have been an incidental finding; those associated with an acute myositis were most likely related to the inflammatory aspects of hemorrhage. Ulcerative dermatitis was an occasional focal lesion indicating the actual epidermal site of injection.

All of the hemorrhage, muscle degeneration and associated inflammation were of unlikely clinical significance and would be expected to heal with no residual morphological or functional alteration.

Appendix F (cont.): PATHOLOGY REPORT

Other lesions present in the lung, digestive tract, lymph nodes and ears were incidental findings and, while they may reflect a concurrent bacterial or parasitic infection, had little to no relationship to the skin and muscle changes.

Case 3 Clipp's Dm phs

for G. DAVID YOUNG, DVM
MAJ, VC
Division of Pathology

19 August 1988/dbj

Appendix F (cont.): PATHOLOGY REPORT

TABLE 1

Grading Criteria for Gross Finding at Injection Sites

1 = 0-0.9 cm²

2 = 1.0-1.9 cm²

3 = 2.0-2.9 cm²

4 = ≥ 3.0 cm²

**GLP 88004
GLOSSARY OF MICROSCOPIC FINDINGS**

SKIN

1. **Hemorrhage** - Variable amounts of red blood cells (RBCs) present within the dermis and/or subcutaneous tissue. Occasional white blood cells (heterophils and monocytes) were scattered among the RBCs. Occasionally associated with the hemorrhagic sites were foci of collagen degradation and infrequent segmental fibrinoid necrosis of the muscular artery wall (site of intra-arterial injection). The degree of hemorrhage was graded on the basis of relative amount of RBCs, expansion of tissue and obliteration of normal skin cytoarchitecture. Severity-grading criteria are as follows:

- 1 = Scattered individual to small aggregates of RBCs coursing between and mildly separating collagen fibers. (Trace)
- 2 = Slightly larger aggregates to islands of RBCs dissecting the dermal collagen and/or subcutaneous tissue, often in a linear fashion, with expansion of the tissue. No to little obliteration of tissue was present. (Mild)
- 3 = Lakes of RBCs that expand dermis and subcutis, often with a bulge in the skin surface contour. Notable cytoarchitectural obliteration was present. Edema, evidenced by clear spaces and widening of collagen/connective tissue fibers, was present. (Moderate)

Appendix F (cont.): PATHOLOGY REPORT

Infiltrate: RBCs with prominent dermal and/or subcutaneous expansion and obliteration, often extending along the entire width of the section. In association with a tunica muscularis, the hemorrhage was often transmural, extending from dermis to subcutis. (Marked)

Severity: (Not observed in this study)

Dermatitis - Presence of inflammatory cells within the dermis and/or subcutaneous tissue. Almost always this condition was present with hemorrhage and in greater numbers than seen with the hemorrhage alone. The inflammatory infiltrate was primarily of two distinct types and were divided into acute and subacute responses.

a. **Acute** - The inflammatory cells consisting predominantly (and often exclusively) of heterophils. Grading was based on the relative numbers of cells present.

- 1 = Scattered cells within and adjacent to sites of hemorrhage. Heterophils were occasionally observed within vascular lumina, often marginated against the endothelium. (Trace)
- 2 = Prominent numbers of cells, often forming small clusters with the dermis and/or subcutis. (Mild)
- 3 = Numerous cells within the dermis and/or subcutis, forming aggregates (microabscesses) up to 1 mm in diameter. Multiple fragments of fur were consistently present within these aggregates. (Moderate)
- 4 = Diffuse infiltration of cells within the dermis and/or subcutis with the complete obliteration of normal structures. (Marked)
- 5 = None (Not observed in this study)

b. **Subacute** - The presence of inflammatory cells consisting of lymphocytes, plasma cells, macrophages and neutrophils. These infiltrates were almost always present in association with resolving hemorrhage. Grading was based on the subjective numbers of cells present.

Appendix F (cont.): PATHOLOGY REPORT

- 1 = Presence of a few mononuclear cells within the dermis and/or subcutis. (Trace)
- 2 = Prominent cell infiltration of the dermis and/or subcutis. (Mild)
- 3 = Diffuse infiltration of the dermis and/or subcutis. (Moderate)
- 4 = Diffuse infiltrate with destruction of dermal and/or subcutaneous structures. (Marked)
- 5 = Severe (Not observed in this study.)

3. Superficial ulcerative dermatitis - This lesion was focally present on the skin surface and consists of an ulcerative, often penetrating lesion with destruction of the epidermis and coagulative necrosis of the superficial dermis (consistent with a needle puncture of the skin). Some sections contained a variably thickened zone of necrotic cellular debris and keratin overlying the ulcer. There was no adjacent inflammation in the epidermis or dermis. Coded as present.

4. Mononuclear cell infiltration - The presence of lymphocytes, plasma cells and macrophages within the dermis. These cells occasionally surrounded adnexa with minimal destruction or obliteration. There was no associated epidermal infiltration nor any adjacent hemorrhage. This minimal infiltration was restricted to the region of the hair tip. Coded as present.

5. Acute folliculitis/perifolliculitis - This minimal and focal lesion consisted of acute inflammation and necrosis of the base of hair follicles and the immediately adjacent dermal tissue. The inflammatory cell infiltrate was composed primarily of heterophils and lymphocytes. Coded as present.

SKELETAL MUSCLE

1. Acute myositis - This was acute inflammation of skeletal muscle. Muscle fibers were separated by infiltration of heterophils and fewer macrophages and lymphocytes. Most cases contained hemorrhage that separated larger muscle bundles and individual muscle fibers. In the more severe cases there was coagulative necrosis of muscle fibers and phagocytosis of the necrotic cellular debris. Criteria for grading severity were based on subjective amount of inflammatory cells and the degree of necrosis.

Appendix F (cont.): PATHOLOGY REPORT

- 1 = Minimal detectable infiltration of heterophils.
(Trace)
- 2 = Mild infiltration of heterophils and few macrophages. (Mild)
- 3 = Prominent heterophilic infiltration with minimal necrosis of skeletal muscle. (Moderate)
- 4 = Diffuse heterophilic infiltration and necrosis of muscle. (Marked)
Severe (Not observed in this study)

Myocyte degeneration - This lesion consists of cellular debris (macrophages, satellite cells) and a scant heterophilic coagulum completely filling and obscuring individual skeletal muscle fibers. There was usually little associated myocyte degeneration and rarely were other inflammatory cells present. The foci of degeneration were often multiple and random within the muscle bundle. This lesion was coded as present when it constituted a significant histological feature.

Muscle

Subacute fibrinous pleuritis - This moderate inflammatory lesion consisted of a diffuse and moderate thickening of the pulmonary pleura by a zone of loosely arrayed fibrin and connective tissue with scattered neovascularization and diffuse infiltration of variable numbers of heterophils, lymphocytes, plasma cells and macrophages. At the junction of pulmonary parenchyma and the thickened pleura were numerous lymphocyte-filled small lymphatic channels. The underlying pulmonary interstitial tissue was mildly thickened and congested with occasional alveoli containing fibrin and edema. This lesion, present in a single animal, is most consistent with a bacterial infection, most likely *Pasteurella multocida*. Coded as present.

Lymph Node

Abscessation - A single mandibular lymph node was infiltrated diffusely by variable numbers of heterophils, lymphocytes, plasma cells and macrophages. Within the tissue was a large focus of degenerative heterophils admixed with cellular necrotic debris which expanded and obliterated the affected lymphoid tissue (abscess). This lesion was surrounded by a minimally compressed zone of edema and a minimal fibrous response. This lesion is most consistent with a bacterial infection, probably *Pasteurella multocida*. Coded as present.

Appendix F (cont.): PATHOLOGY REPORT

CECUM

1. **Mucous cell hyperplasia** - The epithelium contained random and scattered mucous cells. Cecal crypts were diffusely lined by similar cells. The lamina propria contained moderate numbers of plasma cells and few macrophages and lymphocytes. Coded as present.

2. **Plasmacytic infiltration** - This lesion consisted of diffuse and moderate infiltration of the lamina propria by numerous plasma cells and few lymphocytes and macrophages. No epithelial changes were present.

3. **Typhlitis** - This single lesion of the sacculus rotundus of the rabbit cecum consisted of a diffuse expansion of the lamina propria with numerous macrophages, heterophils with fewer lymphocytes and plasma cells. Crypts contained moderate cellular debris, degenerating heterophils and a core of eosinophilic fibrillar material. Within the lymphoid tissue of this tissue, there was a single abscess that obliterated the follicle. Coded as present.

EAR

Fibrinocellular exudate (Acariasis) - Debris removed from the ear canal consisted of abundant fibrinocellular exudate with numerous scattered cross-sections of mites (most probably *Psoroptes cuniculi*). Coded as present.

Appendix F (cont.) : PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH
 DIV OF RES SUPP, PAIR SERV UP
 PRESIDIO OF SAN FRANCISCO, CA 94129
 RABBIT/NEW ZEALAND WHITE

INCIDENCE SUMMARY REPORT FOR GROSS NECROPSY OBSERVATIONS

STUDY NUMBER: 88004P

REPORT INCLUDES ALL SCHEDULED DEATHS

STUDY START DATE: 07-JUN-88

ACUTE/PRIMARY SKIN IRRITATION

	MALES	FEMALES	TOTAL
CECUM			
PARASITIC INFESTATION	4	4	6
DISTENDED, CONTENTS GASEOUS	1	1	0
INFLAMMATION	1	1	0
TOTAL:	6	6	6
EAR			
OTITIS EXTERNA	1	1	1
TOTAL:	1	1	1
LUNG			
LYMPH NODES			
ABCESS(ES)	0	0	1
TOTAL:	0	0	1
MUSCLE			
LUNGS			
PNEUMONIA			
TOTAL:	0	0	1
SKIN			
HEM EAR ANT.	10	11	12
HEM EAR DIST	3	3	6
HEM EAR PROX	1	4	7
HEM THORAX	2	2	5
HEM THIGH	2	4	4
ALOPECIA	1	1	1
FOLLICULITIS	0	0	1
TOTAL:	19	25	36
SKELETAL MUSCLE			
HEM THORAX	0	0	0
HEM THIGH	3	5	5
TOTAL:	3	5	5
THYMUS			
GENERALIZED ATROPHY	1	1	0
TOTAL:	1	1	0

APPENDIX F (cont.) : PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH		INCIDENCE SUMMARY (WITH PERCENTAGES) FOR MICROSCOPIC OBSERVATIONS		PRINTED: 14-DEC-88
DIV OF RES SUPP, PATH SERV GP		STUDY NUMBER: 88004P		PAGE: 1
PRESIDIO OF SAN FRANCISCO, CA 94129		ALL DIAGNOSES		
RABBIT/NEW ZEALAND WHITE		STUDY START DATE: 07-JUN-88		ACUTE/PRIMARY SKIN IRRITATION
NOTES: ANIMALS = ALL SCHEDULED SACRIFICED ANIMAL CONTROLS FROM GROUP(S): 1		ANIMAL SEX: -- MALES --		ACUTE/PRIMARY SKIN IRRITATION
TISSUES WITH DIAGNOSES		DOSAGE GROUP:		
SK EAR DIST		NO. IN GROUP:		
HEMORRHAGE		NUMBER EXAMINED:		
ACUTE DERMATITIS				
ULCERATIVE DERMATITIS				
SUBACUTE DERMATITIS				
SK EAR PROX		NUMBER EXAMINED:		
HEMORRHAGE				
ACUTE DERMATITIS				
ULCERATIVE DERMATITIS				
MONONUCLEAR CELL INFILTRATION				
SUBACUTE DERMATITIS				
SK EAR ARTERY		NUMBER EXAMINED:		
HEMORRHAGE				
ACUTE DERMATITIS				
INTERSTITIAL DERMATITIS				

APPENDIX F (cont.): PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH		INCIDENCE SUMMARY (WITH PERCENTAGES) FOR MICROSCOPIC OBSERVATIONS		PRINTED: 14-DEC-88
DIV OF RES SUPP, PATH SERV GP		STUDY NUMBER: 88004P		PAGE: 2
PRESIDIO OF SAN FRANCISCO, CA 94129		ALL DIAGNOSES		ACUTE/PRIMARY SKIN IRRITATION
RABBIT/NEW ZEALAND WHITE		STUDY START DATE: 07-JUN-88		
NOTES: ANIMALS = ALL SCHEDULED SACRIFICED ANIMALS CONTROLS FROM GROUP(S): 1		ANIMAL SEX:		-- ANIMALS AFFECTED --
TISSUES WITH DIAGNOSES		DOSAGE GROUP:		-- MALES --
SK THORAX	NO. IN GROUP:	C1L5 2 3 4	12 12 12 12
SK THORAX HEMORRHAGE		NUMBER EXAMINED:	11 3 5 3	10% 42% 27%
ACUTE DERMATITIS			0 0 3 2	0% 0% 25% 18%
ACUTE MYOSITIS			0 1 4 0	0% 10% 33% 0%
ACUTE FOLLICULITIS/PERIFOLLICULITIS			0 0 1 0	0% 0% 8% 0%
SKELETAL MUSCLE DEGENERATION			0 2 5 0	0% 20% 42% 0%
ULCERATIVE DERMATITIS			0 1 0 0	0% 10% 0% 0%
SK THIGH	NUMBER EXAMINED:	11 1 12 12	11 6 5 2
HEMORRHAGE			9% 55% 42% 17%	
ACUTE DERMATITIS			0 3 3 0	0% 27% 25% 0%
ACUTE MYOSITIS			1 3 1 0	9% 27% 8% 0%
SKELETAL MUSCLE DEGENERATION			2 1 0 0	18% 9% 0% 0%
ULCERATIVE DERMATITIS			0 0 0 1	0% 0% 0% 1%
EAR DEBRIS	NUMBER EXAMINED:	1 1 1 2	100% 100% 100% 50%
FIBRINOCELLULAR EXUDATE			1 1 1 1	

Table 3 (cont.)

Appendix F (cont.) : PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH
 DIV OF RES SUPP, PATH SERV GP
 PRESIDIO OF SAN FRANCISCO, CA 94129
 RABBIT/NEW ZEALAND WHITE

INCIDENCE SUMMARY OF MICROSCOPIC OBSERVATIONS

STUDY NUMBER: 8004P

NONNEOPLAST C GRADED DIAGNOSES

STUDY START DATE: 07-JUN-88

ACUTE/PRIMARY SKIN IRRITATION

NOTES: ANIMALS = ALL SCHEDULED SACRIFICED ANIMAL CONTROLS FROM GROUP(S): 1	ANIMAL SEX:	ANIMALS AFFECTED --		
TISSUES WITH DIAGNOSES	DOSAGE GROUP:	MALES ..		
	NO. IN GROUP:	C1L5	2	3
SK EAR DIST	NUMBER EXAMINED:	11	11	12
HEMORRHAGE		5	7	10
ACUTE DERMATITIS		1	2	3
SUBACUTE DERMATITIS		3	1	0
SK EAR PROX	NUMBER EXAMINED:	11	11	12
HEMORRHAGE		8	10	9
ACUTE DERMATITIS		5	3	5
SUBACUTE DERMATITIS		1	3	2
SK EAR ARTERY	NUMBER EXAMINED:	11	11	12
HEMORRHAGE		9	10	12
ACUTE DERMATITIS		4	3	8
SUBACUTE DERMATITIS		1	2	0
SK THORAX	NUMBER EXAMINED:	11	10	12
HEMORRHAGE		3	1	5
ACUTE DERMATITIS		0	0	3
ACUTE MYOSITIS		0	1	4
SK THIGH	NUMBER EXAMINED:	11	11	12
HEMORRHAGE		1	6	5
ACUTE DERMATITIS		0	3	3
ACUTE MYOSITIS		1	3	0
EAR DEBRIS	NUMBER EXAMINED:	1	1	1
LUNG	NUMBER EXAMINED:	0	0	1
LYMPH NODE	NUMBER EXAMINED:	0	0	1
SK. MUSCLE THIGH	NUMBER EXAMINED:	2	5	2
HEMORRHAGE		2	4	1
ACUTE MYOSITIS		2	2	0
CECUM	NUMBER EXAMINED:	2	2	0
SKIN (DORSUM)	NUMBER EXAMINED:	0	0	0

NOTE: ENTRIES FLAGGED WITH A - (MINUS) ARE SIGNIFICANTLY DIFFERENT FROM CONTROL AT THE 0.05 LEVEL USING THE KOLMOGOROV-SMIRNOV TWO TAILED TEST.

Table 4

Appendix F (cont.) : PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH DIV OF RES SUPP, PATH SERV GP PRESIDIO OF SAN FRANCISCO, CA 94129		INDIVIDUAL ANIMAL DATA DUMP TABLE STUDY NUMBER: 88004P		PRINTED: 14-DEC-88 PAGE: 1
		STUDY START DATE: 07-JUN-88		ACUTE/PRIMARY SKIN IRRITATION
ANIMAL: 88F0091L	DAY OF DEATH: 4	STATUS: FINAL SACRIFICE		TERMINAL BODY WEIGHT: 3.7 (KGS)
		<< GROSS OBSERVATIONS >>		
(SEVERITY)KEYWORDS		GROSS FREE-TEXT COMMENTS		
SKIN (MODERATE)ALOPECIA				ANTERIOR DORSAL THORAX
		<< NECROPSY MEMOS >>		
TISSUE		NO NECROPSY MEMOS RECORDED ON ANIMAL		
		<< PATHOLOGY OBSERVATIONS >>		HISTOPATHOLOGIC DIAGNOSES / SPECIAL HISTOLOGICAL COMMENTS
TISSUE		DISTRIBUTION (SEVERITY)		
SK EAR PROX		NOT SPECIFIED(MODERATE)		ACUTE DERMATITIS
SK EAR ARTERY		NOT SPECIFIED(PRESENT)		ULCERATIVE DERMATITIS

LETTERMAN ARMY INSTITUTE OF RESEARCH
DIV OF RES SUPP, PATH SERV GP
PRESIDIO OF SAN FRANCISCO, CA 94129
RABBIT/NEW ZEALAND WHITE

APPENDIX F (cont.) : PATHOLOGY REPORT

PRINTED: 14-DEC-88
PAGE: 2
INDIVIDUAL ANIMAL DATA DUMP TABLE
STUDY NUMBER: 88004P

STUDY START DATE: 07-JUN-88
ACUTE/PRIMARY SKIN IRRITATION

ANIMAL: 88F0092L DAY OF DEATH: 3 STATUS: INTERIM SACRIFICE 3

TISSUE (SEVERITY)KEYWORDS << GROSS OBSERVATIONS >>
SKIN (MILD)HEM EAR ART
(TRACE)HEM EAR DIST
CECUM (MARKED)PARASITIC INFESTATION

TISSUE << NECROPSY MEMOS >>
NO NECROPSY MEMOS RECORDED ON ANIMAL

TISSUE DISTRIBUTION (SEVERITY) << PATHOLOGY OBSERVATIONS >>
SK EAR PROX NOT SPECIFIED(TRACE) HISTOPATHOLOGIC DIAGNOSES / SPECIAL HISTOLOGICAL COMMENTS
SK EAR ARTERY NOT SPECIFIED(MODERATE)
SK THIGH NOT SPECIFIED(PRESENT)
CECUM NOT SPECIFIED(PRESENT)
NOT SPECIFIED(PRESENT)

HEMORRHAGE
HEMORRHAGE
SKELETAL MUSCLE DEGENERATION
MUCOUS CELL HYPERPLASIA
PLASMACYTIC INFILTRATION

Appendix F (cont.): PATHOLOGY REPORT

LETTERMAN INSTITUTE OF RESEARCH
 DIV OF RES SUPP, PATH SERV GP
 PRESIDIO OF SAN FRANCISCO, CA 94129
 RABBIT/NEW ZEALAND WHITE

INDIVIDUAL ANIMAL DATA DUMP TABLE
 STUDY NUMBER: 88004P

STUDY START DATE: 07-JUN-88

ANIMAL: 88F00951 DAY OF DEATH: 1

STATUS: INTERIM SACRIFICE 1

ACUTE/PRIMARY SKIN IRRITATION

TISSUE	(SEVERITY)KEYWORDS	<< GROSS OBSERVATIONS >>	GROSS FREE-TEXT COMMENTS
SKIN	(MILD)HEM EAR ART		
	(MILD)HEM THIGH		
EAR	(MILD)OTITIS EXTERNA		

TISSUE	DISTRIBUTION (SEVERITY)	<< PATHOLOGY >>	OBSERVATIONS / HISTOPATHOLOGIC DIAGNOSES / SPECIAL HISTOLOGICAL COMMENTS
SK EAR DIST	NOT SPECIFIED(TRACE)		HEMORRHAGE
SK EAR PROX	NOT SPECIFIED(MILD)		HEMORRHAGE
	NOT SPECIFIED(TRACE)		ACUTE DERMATITIS
SK EAR ARTERY	NOT SPECIFIED(MODERATE)		HEMORRHAGE
	NOT SPECIFIED(TRACE)		ACUTE DERMATITIS
SK THORAX	NOT SPECIFIED(MILD)		HEMORRHAGE
EAR DEBRIS	NOT SPECIFIED(PRESENT)		FIBRINOCELLULAR EXUDATE

NO NECROPSY MEMOS RECORDED ON ANIMAL
 NO NECROPSY MEMOS

TISSUE	DISTRIBUTION (SEVERITY)	<< PATHOLOGY >>	OBSERVATIONS / HISTOPATHOLOGIC DIAGNOSES / SPECIAL HISTOLOGICAL COMMENTS
SK EAR DIST	NOT SPECIFIED(TRACE)		HEMORRHAGE
SK EAR PROX	NOT SPECIFIED(MILD)		HEMORRHAGE
	NOT SPECIFIED(TRACE)		ACUTE DERMATITIS
SK EAR ARTERY	NOT SPECIFIED(MODERATE)		HEMORRHAGE
	NOT SPECIFIED(TRACE)		ACUTE DERMATITIS
SK THORAX	NOT SPECIFIED(MILD)		HEMORRHAGE
EAR DEBRIS	NOT SPECIFIED(PRESENT)		FIBRINOCELLULAR EXUDATE

Appendix F (cont.): PATHOLOGY REPORT

LETERMAN ARMY INSTITUTE OF RESEARCH
 DIV OF RES SUPP, PATH SERV GP
 PRESIDIO OF SAN FRANCISCO, CA 94129
 RABBIT/NEW ZEALAND WHITE

ANIMAL: 88F0096L	DAY OF DEATH: 4	STUDY START DATE: 07-JUN-88	ACUTE/PRIMARY SKIN IRRITATION
		STATUS: FINAL SACRIFICE	TERMINAL BODY WEIGHT: 2.6 (KGS)
<< GROSS OBSERVATIONS >>			
GROSS FREE-TEXT COMMENTS			
TISSUE	(SEVERITY)KEYWORDS		
SKIN	(TRACE)HEM EAR ART		
THYMUS	(MODERATE)GENERALIZED ATROPHY		
CECUM	(MILD)DISTENDED, CONTENTS GASEOUS (MILD)INFLAMMATION	MULTIPLE WHITE SPOTS	
TISSUE	<< NECROPSY MEMOS >>		
NO NECROPSY MEMOS RECORDED ON ANIMAL			
TISSUE	DISTRIBUTION (SEVERITY)	<< PATHOLOGY OBSERVATIONS >>	
SK EAR DIST	NOT SPECIFIED(TRACE)	HISTOPATHOLOGIC DIAGNOSES / SPECIAL HISTOLOGICAL COMMENTS	
CECUM	NOT SPECIFIED(PRESENT) NOT SPECIFIED(PRESENT)	SUBACUTE DERMATITIS MUCOUS CELL HYPERPLASIA TYPHLITIS	

Appendix F (cont.): PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH
 DIV OF RES SUPP, PATH SERV GP
 PRESIDIO OF SAN FRANCISCO, CA 94129
 RABBIT/NEW ZEALAND WHITE

INDIVIDUAL ANIMAL DATA DUMP TABLE
 STUDY NUMBER: 88004P

PRINTED: 14-DEC-88
 PAGE: 5

STUDY START DATE: 07-JUN-88

ACUTE/PRIMARY SKIN IRRITATION

ANIMAL: 88F0100L

DAY OF DEATH: 2

STATUS: INTERIM SACRIFICE 2

TERMINAL BODY WEIGHT: 3.7 (KGS)

TISSUE (SEVERITY)KEYWORDS

<< GROSS OBSERVATIONS >>

GROSS FREE-TEXT COMMENTS

SKIN

(MODERATE)HEM EAR ART

HEM

SKELETAL MUSCLE

(MILD)HEM THIGH

HEM

TISSUE

<< NECROPSY MEMOS >>

<< NECROPSY MEMOS >>

NO NECROPSY MEMOS RECORDED ON ANIMAL

TISSUE	DISTRIBUTION (SEVERITY)	P A T H O L O G Y	O B S E R V A T I O N S	HISTOPATHOLOGIC DIAGNOSES / SPECIAL HISTOLOGICAL COMMENTS
SK EAR PROX	NOT SPECIFIED(MILD)			HEMORRHAGE
SK EAR ARTERY	NOT SPECIFIED(MARKED)			HEMORRHAGE
SK THIGH	NOT SPECIFIED(MILD)			HEMORRHAGE
	NOT SPECIFIED(MILD)			HEMORRHAGE
	NOT SPECIFIED(PRESENT)			ACUTE MYOSITIS
SK. MUSCLE THIGH	NOT SPECIFIED(MILD)			SKELETAL MUSCLE DEGENERATION
	NOT SPECIFIED(MILD)			HEMORRHAGE
	NOT SPECIFIED(PRESENT)			ACUTE MYOSITIS
				SKELETAL MUSCLE DEGENERATION

Appendix F (cont.): PATHOLOGY REPORT

LETTERTMAN ARMY INSTITUTE OF RESEARCH DIV OF RES SUPP, PATH SERV, D PRESIDIO OF SAN FRANCISCO, CA 94129 RABBIT/NEW ZEALAND WHITE		PRINTED: 14-DEC-88 PAGE: 6
ANIMAL: 8BFC104L DAY OF DEATH: 2		STUDY START DATE: 07-JUN-88
		ACUTE/PRIMARY SKIN IRRITATION
		TERMINAL BODY WEIGHT: 3.4 (KGS)
TISSUE (SEVERITY)KEYWORDS		<< GROSS OBSERVATIONS >> GROSS FREE-TEXT COMMENTS
SKIN		(TRACE)HEM THIGH (MILD)HEM THORAX (TRACE)HEM EAR DIST (TRACE)HEM EAR PROX (MILD)HEM EAR ART
TISSUE		<< NECROPSY MEMOS >> NECROPSY MEMOS
NO NECROPSY MEMOS RECORDED ON ANIMAL		
TISSUE DISTRIBUTION (SEVERITY) << PATHOLOGY OBSERVATIONS >> / SPECIAL HISTOLOGICAL COMMENTS		
SK EAR PROX NOT SPECIFIED(MILD) NOT SPECIFIED(TRACE)		
SK EAR ARTERY NOT SPECIFIED(MODERATE) NOT SPECIFIED(TRACE)		
SK THORAX NOT SPECIFIED(TRACE)		

Appendix F (cont.) : PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH DIV OF RES SUPP, PATH SERV GP PRESIDIO OF SAN FRANCISCO, CA 94129 RABBIT/NEW ZEALAND WHITE	INDIVIDUAL ANIMAL DATA DUMP TABLE STUDY NUMBER: 88004P	PRINTED: 14-DEC-88 PAGE: 7
ANIMAL: 88F0105L	STUDY START DATE: 07-JUN-88	ACUTE/PRIMARY SKIN IRRITATION
DAY OF DEATH: 3	STATUS: INTERIM SACRIFICE 3	TERMINAL BODY WEIGHT: 3.8 (KGS)
TISSUE (SEVERITY)KEYWORDS	<< GROSS OBSERVATIONS >> GROSS FREE-TEXT COMMENTS	
SKIN (TRACE)HEM EAR ART (TRACE)HEM EAR DIST (MILD)HEM THORAX		
SKELETAL MUSCLE (MILD)HEM THIGH		
CECUM (MARKED)PARASITIC INFESTATION		
TISSUE NO NECROPSY MEMOS RECORDED ON ANIMAL	<< NECROPSY MEMOS >> NECROPSY MEMOS	NECROPSY MEMOS
TISSUE NO NECROPSY MEMOS RECORDED ON ANIMAL	DISTRIBUTION (SEVERITY) SK EAR DIST NOT SPECIFIED(TRACE) NOT SPECIFIED(TRACE)	OBSERVATIONS / HISTOPATHOLOGIC DIAGNOSES / SPECIAL HISTOLOGICAL COMMENTS HEMORRHAGE SUBACUTE DERMATITIS
SK EAR PROX NOT SPECIFIED(MILD) NOT SPECIFIED(TRACE)		HEMORRHAGE SUBACUTE DERMATITIS
SK EAR ARTERY NOT SPECIFIED(MODERATE) NOT SPECIFIED(TRACE)		HEMORRHAGE SUBACUTE DERMATITIS
SK THORAX NOT SPECIFIED(TRACE)		HEMORRHAGE

APPENDIX F (cont.): PATHOLOGY REPORT

U.S. ARMY INSTITUTE OF RESEARCH
DIV OF MED SUPP, PATH SERV, SP
PRECIO OF SAN FRANCISCO, CA 94124
RABBIT/NEW ZEALAND WHITE

INDIVIDUAL ANIMAL DATA DUMP TABLE
STUDY NUMBER: 88004P

STUDY START DATE: 07-JUN-88

ANIMAL: 88004P DAY OF DEATH: 4 STATUS: FINAL SACRIFICE

PRINTED: 14-DEC-88
PAGE: 8

ACUTE/PRIMARY SKIN IRRITATION

TERMINAL BODY WEIGHT: 4.0 (KGS)

TISSUE (SEVERITY)KEYWORDS

<< G R O S S O B S E R V A T I O N S >>

GROSS FREE-TEXT COMMENTS

SKIN (TRACE)HEM EAR ART

<< N E C R O S Y M E M O S >>

NECROPSY MEMOS

TISSUE
NO NECROPSY MEMOS RECORDED ON ANIMAL

TISSUE DISTRIBUTION (SEVERITY)

<< P A T H O L O G Y O B S E R V A T I O N S >>

HISTOPATHOLOGIC DIAGNOSES / SPECIAL HISTOLOGICAL COMMENTS

SK EAR DIST NOT SPECIFIED(MILD)
NOT SPECIFIED(TRACE)

SK EAR PROX NOT SPECIFIED(TRACE)
NOT SPECIFIED(TRACE)

SK EAR ARTERY NOT SPECIFIED(MILD)
NOT SPECIFIED(TRACE)

HEMORRHAGE SUBACUTE DERMATITIS

HEMORRHAGE ACUTE DERMATITIS

HEMORRHAGE ACUTE DERMATITIS

Appendix F (cont.) : PATHOLOGY REPORT

LETTERMAN ARA, INSTITUTE OF RESEARCH
DOY, OF RES SUPP, PATH SERV GP
PRESSOIO JF SAN FRANCISCO, CA 94129
PRABBIT/NEW ZEALAND WHITE

INDIVIDUAL ANIMAL DATA DUMP TABLE
STUDY NUMBER: 8801_P

PRINTED: 14-DEC-88
PAGE: 9

STUDY START DATE: 07-JUN-88 ACUTE/PRIMARY SKIN IRRITATION

ANIMAL: 88FC107L DAY OF DEATH: 2 STATUS: INTERIM SACRIFICE 2 TERMINAL BODY WEIGHT: 3.7 (KGS)

(SEVERITY)KEYWORDS : ISSUE : GROSS SKEWATIONS :> GROSS FREE-TEXT COMMENTS

HEAVY INFESTATION OF WHIPWORMS (MARKED) PARASITIC INFESTATION

NECROPSY MEMOS
ISSUE

<< PATHOLOGY OBSERVATIONS >>

SK EAR DIST

SK EAR PROX	NOT SPECIFIED(TRACE)	HEMORRHAGE
SK EAR ARTERY	NOT SPECIFIED(MODERATE)	HEMORRHAGE
	NOT SPECIFIED(PRESENT)	ULCERATIVE DERMATITIS

Appendix F (cont.) : PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH
DIV OF RES SUPP, PATH SERV CO
FRESIDIO OF SAN FRANCISCO, CA 94129
RABBIT/NEW ZEALAND WHITE

PRINTED: 14-DEC-88
PAGE: 10
INDIVIDUAL ANIMAL DATA DUMP TABLE:

STUDY STUDY NUMBER: 88004P

STUDY START DATE: 07-JUN-88

ACUTE/PRIMARY SKIN IRRITATION

DAY OF DEATH: 1 STATUS: INTERIM SACRIFICE 1

TERMINAL BODY WEIGHT: 3.4 (KGS)

(SEVERITY)KEYWORDS << G R O S S O B S E R V A T I O N S >>

TISSUE SKIN GROSS FREE-TEXT COMMENTS

(TRACE)HEM EAR ART

<< N E C R O P S Y M E M O S >>

NECROPSY MEMOS

NO NECROPSY MEMOS RECORDED ON ANIMAL

TISSUE DISTRIBUTION (SEVERITY) << P A T H O L O G Y O B S E R V A T I O N S >>

SK EAR PROX NOT SPECIFIED(MILD)

NOT SPECIFIED(TRACE)

SK EAR ARTERY NOT SPECIFIED(MODERATE)

NOT SPECIFIED(TRACE)

PATHOLOGY HISTOPATHOLOGIC DIAGNOSES / SPECIAL HISTOLOGICAL COMMENTS

SK EAR PROX HEMORRHAGE

ACUTE DERMATITIS

SK EAR ARTERY HEMORRHAGE

ACUTE DERMATITIS

Appendix F (cont.) : PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH
 DIV OF RES SUPP, PATH SERV GP
 PRESIDIO OF SAN FRANCISCO, CA 94129
 RABBIT/NEW ZEALAND WHITE

INDIVIDUAL ANIMAL DATA DUMP TABLE
 STUDY NUMBER: 88004P

PRINTED: 14-DEC-88
 PAGE: 11

STUDY START DATE: 07-JUN-88

ACUTE/PRIMARY SKIN IRRITATION

ANIMAL: 88F0112L

DAY OF DEATH: 3 STATUS: INTERIM SACRIFICE 3

TERMINAL BODY WEIGHT: 3.1 (KGS)

TISSUE	(SEVERITY)KEYWORDS	<< GROSS OBSERVATIONS >>	GROSS FREE-TEXT COMMENTS
SKIN	(TRACE)HEM EAR ART		
SKELETAL MUSCLE	(MILD)HEM THIGH		
CECUM	(MILD)PARASITIC INFESTATION		
		<< NECROPSY MEMOS >>	NECROPSY MEMOS
TISSUE			
NO NECROPSY MEMOS RECORDED ON ANIMAL			
TISSUE	DISTRIBUTION (SEVERITY)	P A T H O L O G Y	O B S E R V A T I O N S > HISTOPATHOLOGIC DIAGNOSES / SPECIAL HISTOLOGICAL COMMENTS
SK EAR DIST	NOT SPECIFIED(TRACE) NOT SPECIFIED(TRACE)		HEMORRHAGE ACUTE DERMATITIS
SK EAR ARTERY	NOT SPECIFIED(MODERATE)		HEMORRHAGE
SK. MUSCLE THIGH	NOT SPECIFIED(TRACE) NOT SPECIFIED(TRACE) NOT SPECIFIED(PRESENT)		HEMORRHAGE ACUTE MYOSITIS SKELETAL MUSCLE DEGENERATION

Appendix F (cont.): PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH DIV OF RES SUPP, PATH SERV GP PRESIDIO OF SAN FRANCISCO, CA 94129 RABBIT/NEW ZEALAND WHITE	ANIMAL: 88F0091R DAY OF DEATH:	TISSUE	SKIN	(SEVERITY)KEYWORDS
--	-------------------------------------	--------	------	--------------------

INDIVIDUAL ANIMAL DATA DUMP TABLE
STUDY NUMBER: 880004P
PRINTED: 14-DEC-88
PAGE: 13

TERMINAL BODY WEIGHT: 3.7 (KGS)
FINAL SACRIFICE

OBSERVATIONS >
GROSS FREE-TEXT COMMENTS

卷之三

ANTERIOR DORSAL THORAX

R O P S Y N E M E N O S A A

卷之三

HISTOPATHOLOGIC DIAGNOSES / SPECIAL HISTIOLOGICAL COMMENTS

卷之三

HEMORRHAGE **SUBACUTE DERMATITIS**

HEMORRHAGE

ULCERATIVE DERMALITIS

卷之二十一

卷之三

APPENDIX F (cont.) : PATHOLOGY REPORT

LETTERRMAN ARMY INSTITUTE OF RESEARCH
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 PRESIDIO OF SAN FRANCISCO, CA 94129
 RABBIT/NEW ZEALAND WHITE

ANIMAL: 88F0092R DAY OF DEATH: 3

INDIVIDUAL ANIMAL DATA DUMP TABLE
 STUDY NUMBER: 88004P

STUDY START DATE: 07-JUN-88

ACUTE/PRIMARY SKIN IRRITATION

TERMINAL BODY WEIGHT: 3.4 (KGS)

PRINTED: 14-DEC-88
 PAGE: 14

TISSUE	(SEVERITY)KEYWORDS	<< GROSS OBSERVATIONS >> GROSS FREE-TEXT COMMENTS	<< STATUS: INTERIM SACRIFICE 3 >>
SKIN	(MILD)HEM EAR ART (TRACE)HEM EAR PROX		
SKELETAL MUSCLE	(MODERATE)HEM THIGH		
CECUM	(MARKED)PARASITIC INFESTATION		
TISSUE		<< NECROPSY MEMOS >> NECROPSY MEMOS	
NO NECROPSY MEMOS RECORDED ON ANIMAL			
TISSUE	DISTRIBUTION (SEVERITY)	<< PATHOLOGY OBSERVATIONS >> HISTOPATHOLOGIC DIAGNOSES / SPECIAL HISTOLOGICAL COMMENTS	
SK EAR DIST	NOT SPECIFIED(TRACE)		HEMORRHAGE
SK EAR PROX	NOT SPECIFIED(MILD)		HEMORRHAGE
SK EAR ARTERY	NOT SPECIFIED(MODERATE)		HEMORRHAGE
	NOT SPECIFIED(TRACE)		SUBACUTE DERMATITIS
SK THIGH	NOT SPECIFIED(MILD)		HEMORRHAGE
	NOT SPECIFIED(MODERATE)		ACUTE DERMATITIS
	NOT SPECIFIED(TRACE)		ACUTE MYOSITIS
	NOT SPECIFIED(PRESENT)		SKELETAL MUSCLE DEGENERATION
SK. MUSCLE THIGH	NOT SPECIFIED(TRACE)		ACUTE MYOSITIS
	NOT SPECIFIED(PRESENT)		SKELETAL MUSCLE DEGENERATION
CECUM	NOT SPECIFIED(PRESENT)		MUCOUS CELL HYPERPLASIA
	NOT SPECIFIED(PRESENT)		PLASMACYTIC INFILTRATION

Appendix F (cont.) : PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH
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 PRESIDIO OF SAN FRANCISCO, CA 94129
 RABBIT/NEW ZEALAND WHITE

ANIMAL: 8800095R DAY OF DEATH: 1 STATUS: INTERIM SACRIFICE 1

TISSUE (SEVERITY)KEYWORDS << G R O S S O B S E R V A T I O N S >>
 SKIN (MODERATE)HEM EAR ART
 (TRACE)HEM THORAX

SKELETAL MUSCLE (MILD)HEM THIGH
 EAR (MILD)OTITIS EXTERNA

TISSUE << N E C R O P S Y M E M O S >>
 NO NECROPSY MEMOS

TISSUE DISTRIBUTION (SEVERITY) << P A T H O L O G Y O B S E R V A T I O N S >>
 NO NECROPSY MEMOS RECORDED ON ANIMAL

TISSUE	DISTRIBUTION (SEVERITY)	PATHOLOGY	OBSERVATIONS	HISTOPATHOLOGIC DIAGNOSES / SPECIAL HISTOLOGICAL COMMENTS
SK EAR PROX	NOT SPECIFIED(MILD) NOT SPECIFIED(TRACE)		HEMORRHAGE ACUTE DERMATITIS	
SK EAR ARTERY	NOT SPECIFIED(MARKED) NOT SPECIFIED(MODERATE)		HEMORRHAGE ACUTE DERMATITIS	
SK THORAX	NOT SPECIFIED(MODERATE)		TISSUE IS MISSING	
SK THIGH	NOT SPECIFIED(MODERATE) NOT SPECIFIED(MILD) NOT SPECIFIED(MILD)		HEMORRHAGE ACUTE DERMATITIS ACUTE MYOSITIS	
EAR DEBRIS	NOT SPECIFIED(PRESENT)		FIBRINOCELLULAR EXUDATE	

Appendix F (cont.) : PATHOLOGY REPORT

LETTERTMAN ARMY INSTITUTE OF RESEARCH
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 PRESIDIO OF SAN FRANCISCO, CA 94129
 RABBIT/NEW ZEALAND WHITE

INDIVIDUAL ANIMAL DATA DUMP TABLE
 STUDY NUMBER: 88004P

STUDY START DATE: 07-JUN-88

ACUTE/PRIMARY SKIN IRRITATION

ANIMAL:	DAY OF DEATH:	DAY:	STATUS:	FINAL SACRIFICE	TERMINAL BODY WEIGHT:	2.6 (KGS)
			<< G R O S S O B S E R V A T I O N S >>			
			GROSS OBSERVATIONS			
			GROSS FREE TEXT COMMENTS			
SKIN			(TRACE)HEM EAR ART			
THYMUS			(MODERATE)GENERALIZED ATROPHY			
CECUM			(WILD)DISTENDED, CONTENTS GASEOUS			
			(WILD)INFLAMMATION			
			MULTIPLE WHITE SPOTS			
			<< N E C R O P S Y M E M O S >>			
			NECROPSY MEMOS			
			NECROPSY MEMOS			
TISSUE			NO NECROPSY MEMOS RECORDED ON ANIMAL			
			<< P A T H O L O G Y O B S E R V A T I O N S >>			
			PATHOLOGY OBSERVATIONS			
			HISTOPATHOLOGIC DIAGNOSES / SPECIAL HISTOLOGICAL COMMENTS			
SK EAR DIST			DISTRIBUTION (SEVERITY)			
CECUM			NOT SPECIFIED(TRACE)			
			NOT SPECIFIED(PRESENT)			
			NOT SPECIFIED(PRESENT)			
			NOT SPECIFIED(PRESENT)			
			SUBACUTE DERMATITIS			
			MUCOUS CELL HYPERPLASIA			
			TYPHLITIS			

APPENDIX F (cont.): PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH
 DIV OF RES SUPP, PATH SERV GP
 PRESIDIO OF SAN FRANCISCO, CA 94129
 RABBIT/NEW ZEALAND WHITE

INDIVIDUAL ANIMAL DATA DUMP TABLE
 STUDY NUMBER: 88004P
 PRINTED: 14-DEC-88
 PAGE: 17

STUDY START DATE: 07-JUN-88

STUDY END DATE: 07-JUN-88

ANIMAL: 88F0100R DAY OF DEATH: 2 STATUS: INTERIM SACRIFICE 2

TERMINAL BODY WEIGHT: 3.7 (KGS)

ACUTE/PRIMARY SKIN IRRITATION

TISSUE (SEVERITY)KEYWORDS << GROSS OBSERVATIONS >>

GROSS FREE-TEXT (COMMENTS)

SKIN (MODERATE)HEM EAR ART

(MILD)HEM THIGH

(MILD)HEM MUSCLE

(MILD)HEM THIGH

(MILD)HEM MUSCLE

(MILD)HEM THIGH

(MILD)HEM MUSCLE

(MILD)HEM THIGH

(MILD)HEM MUSCLE

(MILD)HEM THIGH

(MILD)HEM MUSCLE

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(MILD)HEM MUSCLE

(MILD)HEM THIGH

(MILD)HEM MUSCLE

(MILD)HEM THIGH

(MILD)HEM MUSCLE

(MILD)HEM THIGH

(MILD)HEM MUSCLE

NO NECROPSY MEMOS RECORDED ON ANIMAL

TISSUE	DISTRIBUTION (SEVERITY)	PATHOLOGY	OBSERVATIONS	HISTOPATHOLOGIC DIAGNOSES / SPECIAL HISTOLOGICAL COMMENTS
SK EAR DIST	NOT SPECIFIED(MODERATE)			HEMORRHAGE
SK EAR PROX	NOT SPECIFIED(MILD)			HEMORRHAGE
SK EAR ARTERY	NOT SPECIFIED(MODERATE)			HEMORRHAGE
SK THORAX	NOT SPECIFIED(TRACE)			HEMORRHAGE ACUTE DERMATITIS
SK. MUSCLE THIGH	NOT SPECIFIED(TRACE) NOT SPECIFIED(PRESENT)			ACUTE MYOSITIS SKELETAL MUSCLE DEGENERATION
	NOT SPECIFIED(TRACE) NOT SPECIFIED(PRESENT)			HEMORRHAGE SKELETAL MUSCLE DEGENERATION

Appendix F (cont.): PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH
 DIV OF RES SUPP, PATH SERV GP
 PRESIDIO OF SAN FRANCISCO, CA 94129
 RABBIT/NEW ZEALAND WHITE

ANIMAL: 88F0104R DAY OF DEATH: 2 STUDY START DATE: 07-JUN-88

(SEVERITY)KEYWORDS
 SKIN (MILD)HEM EAR ART
 (TRACE)HEM EAR DIST
 (TRACE)HEM EAR PROX
 (TRACE)HEM THIGH

TISSUE NO NECROPSY MEMOS
 NO NECROPSY MEMOS RECORDED ON ANIMAL

INDIVIDUAL ANIMAL DATA DUMP TABLE
 STUDY NUMBER: 88004P

ACUTE/PRIMARY SKIN IRRITATION

STUDY START DATE: 07-JUN-88

ANIMAL: 88F0104R DAY OF DEATH: 2 STATUS: INTERIM SACRIFICE 2

<< G R O S S O B S E R V A T I O N S >>
 GROSS FREE-TEXT COMMENTS

<< N E C R O P S Y M E M O S >>
 NECROPSY MEMOS

<< P A T H O L O G Y O B S E R V A T I O N S >>
 HISTOPATHOLOGIC DIAGNOSES / SPECIAL HISTOLOGICAL COMMENTS

SK EAR DIST	NOT SPECIFIED(MILD)	HEMORRHAGE
	NOT SPECIFIED(PRESENT)	ULCERATIVE DERMATITIS
SK EAR PROX	NOT SPECIFIED(MILD)	HEMORRHAGE
SK EAR ARTERY	NOT SPECIFIED(MODERATE)	HEMORRHAGE
SK THORAX	NOT SPECIFIED(TRACE)	HEMORRHAGE
	NOT SPECIFIED(PRESENT)	SKELETAL MUSCLE DEGENERATION
SK THIGH	NOT SPECIFIED(TRACE)	HEMORRHAGE

Appendix F (cont.) : PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH
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 PRESIDIO OF SAN FRANCISCO, CA 94129
 RABBIT/NEW ZEALAND WHITE

PRINTED: 14-DEC-88

PAGE: 19

INDIVIDUAL ANIMAL DATA DUMP TABLE

STUDY NUMBER: 88004P

STUDY START DATE: 07-JUN-88

ACUTE/PRIMARY SKIN IRRITATION

ANIMAL: 8800105R	DAY OF DEATH:	3	STATUS: INTERIM SACRIFICE 3	TERMINAL BODY WEIGHT: 3.8 (KGS)
TISSUE	(SEVERITY)KEYWORDS	<< GROSS OBSERVATIONS >>	GROSS FREE-TEXT COMMENTS	
SKIN	(MILD)HEM EAR ART (TRACE)HEM EAR DIST (TRACE)HEM EAR PROX			
CECUM	(MARKED)PARASITIC INFESTATION			
		<< NECROPSY MEMOS >>	NECROPSY MEMOS	
TISSUE	NO NECROPSY MEMOS FOR CORDED ON ANIMAL			
		<< PATHOLOGY OBSERVATIONS >>	HISTOPATHOLOGIC DIAGNOSES / SPECIAL HISTOLOGICAL COMMENTS	
TISSUE	DISTRIBUTION (SEVERITY)			
SK EAR DIST	NOT SPECIFIED(MILD)		HEMORRHAGE	
SK EAR PROX	NOT SPECIFIED(TRACE)		HEMORRHAGE	
	NOT SPECIFIED(TRACE)		SUBACUTE DERMATITIS	
SK EAR ARTERY	NOT SPECIFIED(MARKED)		HEMORRHAGE	
	NOT SPECIFIED(TRACE)		SUBACUTE DERMATITIS	
SK. MUSCLE THIGH	NOT SPECIFIED(MILD)		HEMORRHAGE	
	NOT SPECIFIED(TRACE)		ACUTE MYOSITIS	
	NOT SPECIFIED(PRESENT)		SKELETAL MUSCLE DEGENERATION	

Appendix F (cont.): PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH
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 PRESIDIO OF SAN FRANCISCO, CA 94129
 RABBIT/NEW ZEALAND WHITE

PRINTED: 14-DEC-88
 PAGE: 20
 INDIVIDUAL ANIMAL DATA DUMP TABLE
 STUDY NUMBER: 88004P

STUDY START DATE: 07-JUN-88 ACUTE/PRIMARY SKIN IRRITATION

ANIMAL: 8810106R DAY OF DEATH: 4 STATUS: FINAL SACRIFICE TERMINAL BODY WEIGHT: 4.0 (KGS)

TISSUE (SEVERITY)KEYWORDS << GROSS OBSERVATIONS >>
 GROSS FREE-TEXT COMMENTS

SKIN
 (TRACE)HEM EAR ART
 (TRACE)HEM EAR DIST
 (TRACE)HEM EAR PROX

<< NECROPSY MEMOS >>
 NECROPSY MEMOS

TISSUE
 NO NECROPSY MEMOS RECORDED ON ANIMAL

TISSUE DISTRIBUTION (SEVERITY) << PATHOLOGY OBSERVATIONS >>
 HISTOPATHOLOGIC DIAGNOSES / SPECIAL HISTOLOGICAL COMMENTS

SK EAR PROX NOT SPECIFIED(MILD)
 NOT SPECIFIED(TRACE)

SK EAR ARTERY NOT SPECIFIED(MILD)

HEMORRHAGE
 SUBACUTE DERMATITIS
 HEMORRHAGE

Appendix F (cont.) : PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH
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 PRESIDIO OF SAN FRANCISCO, CA 94129
 RABBIT/NEW ZEALAND WHITE

INDIVIDUAL ANIMAL DATA DUMP TABLE
 STUDY NUMBER: 88064P

STUDY START DATE: 07-JUN-88

ACUTE/PRIMARY SKIN IRRITATION

ANIMAL:	DAY OF DEATH:	STATUS:	INTERIM SACRIFICE	TERMINAL BODY WEIGHT:
88F0109R	1	<< GROSS OBSERVATIONS >>		3.4 (KGS)
TISSUE	(SEVERITY)KEYWORDS	GROSS FREE-TEXT COMMENTS		
SKIN	(MILD)HEM EAR ART (TRACE)HEM THIGH (TRACE)HEM THORAX			
TISSUE	<< NECROPSY MEMOS >>			
NO NECROPSY MEMOS RECORDED ON ANIMAL				
TISSUE	DISTRIBUTION (SEVERITY)	<< PATHOLOGY	OBSERVATIONS	HISTOPATHOLOGIC DIAGNOSES / SPECIAL HISTOLOGICAL COMMENTS
SK EAR DIST	NOT SPECIFIED(MILD) NOT SPECIFIED(TRACE)			HEMORRHAGE ACUTE DERMATITIS
SK EAR PROX	NOT SPECIFIED(MODERATE) NOT SPECIFIED(TRACE)			HEMORRHAGE ACUTE DERMATITIS
SK EAR ARTERY	NOT SPECIFIED(MARKED) NOT SPECIFIED(MODERATE) NOT SPECIFIED(PRESENT)			HEMORRHAGE ACUTE DERMATITIS ULCERATIVE DERMATITIS
SK THIGH	NOT SPECIFIED(TRACE) NOT SPECIFIED(TRACE) NOT SPECIFIED(TRACE)			HEMORRHAGE ACUTE DERMATITIS ACUTE MYOSITIS

Appendix F (cont.) : PATHOLOGY REPORT

LETTERMAN INSTITUTE OF RESEARCH
 DIV OF RES SUPP, PATH SERV GP
 PRESIDIO OF SAN FRANCISCO, CA 94129
 RABBIT/NEW ZEALAND WHITE

INDIVIDUAL ANIMAL DATA DUMP TABLE
 STUDY NUMBER: 88004P

STUDY START DATE: 07-JUN-88

ACUTE/PRIMARY SKIN IRRITATION

ANIMAL: 8800112R	DAY OF DEATH:	3	STATUS: INTERIM SACRIFICE 3	TERMINAL BODY WEIGHT: 3.1 (KGS)
			<< GROSS OBSERVATIONS >>	GROSS FREE-TEXT COMMENTS
TISSUE	(SEVERITY)KEYWORDS			
SKIN	(MILD)HEM THIGH (TRACE)HEM EAR ART			
SKELETAL MUSCLE	(MILD)HEM THIGH			
CECUM	(MILD)PARASITIC INFESTATION			
			<< NECROPSY MEMOS >>	NECROPSY MEMOS
TISSUE	NO NECROPSY MEMOS RECORDED ON ANIMAL			
			<< PATHOLOGY OBSERVATIONS >>	HISTOPATHOLOGIC DIAGNOSES / SPECIAL HISTOLOGICAL COMMENTS
TISSUE	DISTRIBUTION (SEVERITY)			
SK EAR DIST	NOT SPECIFIED(TRACE)			HEMORRHAGE
SK EAR PROX	NOT SPECIFIED(MILD)			HEMORRHAGE
SK EAR ARTERY	NOT SPECIFIED(MODERATE)			HEMORRHAGE
SK THORAX	NOT SPECIFIED(PRESENT)			ULCERATIVE DERMATITIS
SK THIGH	NOT SPECIFIED(MILD)			HEMORRHAGE
SK. MUSCLE THIGH	NOT SPECIFIED(MILD)			HEMORRHAGE
	NOT SPECIFIED(PRESENT)			SKELETAL MUSCLE DEGENERATION

Appendix F (cont.): PATHOLOGY REPORT

LETERMAN ARMY INSTITUTE OF RESEARCH
 DIV OF RES SUPP, PATH SERV GP
 PRESIDIO OF SAN FRANCISCO, CA 94129
 RABBIT/NEW ZEALAND WHITE

INDIVIDUAL ANIMAL DATA DUMP TABLE
 STUDY NUMBER: 88004P

STUDY START DATE: 07-JUN-88

ACUTE/PRIMARY SKIN IRRITATION

ANIMAL: 8BF014R DAY OF DEATH: -2 STATUS: FOUND DEAD

TERMINAL BODY WEIGHT: ---

TISSUE (SEVERITY)KEYWORDS
 NO GROSS OBSERVATIONS RECORDED ON ANIMAL

<< NECROPSY MEMOS >>
 NECROPSY MEMOS

This animal died before the start of the study, and was not included in any data tabulation.

TISSUE DISTRIBUTION (SEVERITY) << PATHOLOGY OBSERVATIONS HISTOPATHOLOGIC DIAGNOSES / SPECIAL HISTOLOGICAL COMMENTS

SK EAR DIST

REQUIRED TISSUE NOT EXAMINED

SK EAR PROX

REQUIRED TISSUE NOT EXAMINED

SK EAR ARTERY

REQUIRED TISSUE NOT EXAMINED

SK THORAX

REQUIRED TISSUE NOT EXAMINED

SK THIGH

REQUIRED TISSUE NOT EXAMINED

Appendix F (cont.): PATHOLOGY REPORT

LETERMAN ARMY INSTITUTE OF RESEARCH
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 RABBIT/NEW ZEALAND WHITE

		INDIVIDUAL ANIMAL DATA DUMP TABLE		PRINTED: 14-DEC-88	PAGE: 25
		STUDY NUMBER: 88004P		ACUTE/PRIMARY SKIN IRRITATION	
		STUDY START DATE: 07-JUN-88		TERMINAL BODY WEIGHT: 3.2 (KGS)	
ANIMAL: 88F0093R	DAY OF DEATH:	2	STATUS: INTERIM SACRIFICE 2	GROSS OBSERVATIONS	>> GROSS FREE-TEXT COMMENTS
TISSUE	(SEVERITY)KEYWORDS				
SKIN	(TRACE)HEM EAR ART (TRACE)HEM EAR DIST (TRACE)HEM EAR PROX (MODERATE)HEM THORAX (MODERATE)HEM THIGH				
TISSUE			<< NECROPSY MEMOS >>		
NO NECROPSY MEMOS RECORDED ON ANIMAL					
TISSUE	DISTRIBUTION (SEVERITY)	<< PATHOLOGY	OBSERVATIONS >>	HISTOPATHOLOGIC DIAGNOSES / SPECIAL HISTOLOGICAL COMMENTS	
SK EAR DIST	NOT SPECIFIED(MILD)			HEMORRHAGE	
SK EAR PROX	NOT SPECIFIED(MODERATE)			HEMORRHAGE	
SK EAR ARTERY	NOT SPECIFIED(TRACE)			ACUTE DERMATITIS	
SK THORAX	NOT SPECIFIED(MILD)			HEMORRHAGE	
SK THIGH	NOT SPECIFIED(MARKED) NOT SPECIFIED(MILD) NOT SPECIFIED(MILD) NOT SPECIFIED(PRESENT)			HEMORRHAGE ACUTE DERMATITIS ACUTE MYOSITIS SKELETAL MUSCLE DEGENERATION HEMORRHAGE ACUTE DERMATITIS	

Appendix F (cont.): PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH DIV OF RES SUPP, PATH SERV GP PRESIDIO OF SAN FRANCISCO, CA 94129 RABBIT/NEW ZEALAND WHITE		PRINTED: 14-DEC-88 PAGE: 26
ANIMAL: 88F0094R		INDIVIDUAL ANIMAL DATA DUMP TABLE STUDY NUMBER: 88004P
DAY OF DEATH: 2		STUDY START DATE: 07-JUN-88 ACUTE/PRIMARY SKIN IRRITATION
TISSUE (SEVERITY)KEYWORDS		TERMINAL BODY WEIGHT: 3.1 (KGS)
SKIN		
(MILD)HEM EAR ART (TRACE)HEM EAR DIST (TRACE)HEM EAR PROX (MILD)HEM THIGH		
(TRACE)HEM THIGH		
(MILD)OTITIS EXTERNA		
<< GROSS OBSERVATIONS >> GROSS FREE-TEXT COMMENTS		
SKELETAL MUSCLE		
CAR		
<< NECROPSY MEMOS >> NECROPSY MEMOS		
TISSUE		
NO NECROPSY MEMOS RECORDED ON ANIMAL		
<< PATHOLOGY DISTRIBUTION (SEVERITY) >>		
TISSUE		
SK EAR PROX		
NOT SPECIFIED(MODERATE) NOT SPECIFIED(TRACE) NOT SPECIFIED(PRESENT)		
SK EAR ARTERY		
NOT SPECIFIED(MARKED) NOT SPECIFIED(MILD)		
SK THIGH		
NOT SPECIFIED(MILD)		
EAR DEBRIS		
NOT SPECIFIED(PRESENT)		
<< OBSERVATIONS >> HISTOPATHOLOGIC DIAGNOSES / SPECIAL HISTOLOGICAL COMMENTS		
TISSUE		
SK EAR PROX		
HEMORRHAGE ACUTE DERMATITIS MONONUCLEAR CELL INFILTRATION		
SK EAR ARTERY		
HEMORRHAGE ACUTE DERMATITIS		
SK THIGH		
HEMORRHAGE		
EAR DEBRIS		
FIBRINOCELLULAR EXUDATE		

Appendix F (cont.): PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH DIV OF RES SUPP, PATH SERV GP PRESIDIO OF SAN FRANCISCO, CA 94129 RABBIT/NEW ZEALAND WHITE		INDIVIDUAL ANIMAL DATA DUMP TABLE STUDY NUMBER: 88004P		PRINTED: 14-DEC-88 PAGE: 27	
ANIMAL: 88F0098R	DAY OF DEATH: 4	STUDY START DATE: 07 JUN-88	ACUTE/PRIMARY SKIN IRRITATION		
TISSUE	(SEVERITY)KEYWORDS	STATUS: FINAL SACRIFICE	TERMINAL BODY WEIGHT:		
SKIN	(TRACE)HEM EAR ART (TRACE)HEM EAR PROX (MILD)FOLLICULITIS (MILD)PARASITIC INFESTATION	<< G R O S S O B S E R V A T I O N S >> GROSS FREE-TEXT COMMENTS	3.2 (KGS)		
CECUM					
TISSUE		<< N E C R O P S Y M E M O S >>			
NO NECROPSY MEMOS RECORDED ON ANIMAL					
TISSUE	DISTRIBUTION (SEVERITY)	<< P A T H O L O G Y O B S E R V A T I O N S >>	O B S E R V A T I O N S / HISTOPATHOLOGIC DIAGNOSES / SPECIAL HISTOLOGICAL COMMENTS		
SK EAR PROX	NOT SPECIFIED(MILD)		HEMORRHAGE		
SK EAR ARTERY	NOT SPECIFIED(MILD)		HEMORRHAGE		
SK THORAX	NOT SPECIFIED(TRACE)		ACUTE DERMATITIS		
	NOT SPECIFIED(PRESENT)		SKELETAL MUSCLE DEGENERATION		

Appendix F (cont.): PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH
 DIV OF RES SUPP, PATH SERV GP
 PRESIDIO OF SAN FRANCISCO, CA 94129
 RABBIT/NEW ZEALAND WHITE

INDIVIDUAL ANIMAL DATA DUMP TABLE
 STUDY NUMBER: 88004P

STUDY START DATE: 07-JUN-88

ACUTE/PRIMARY SKIN IRRITATION

ANIMAL: 88F009R DAY OF DEATH: 3 STATUS: INTERIM SACRIFICE 3

TISSUE (SEVERITY)KEYWORDS << GROSS OBSERVATIONS >>
 SKIN (MILD)HEM EAR ART
 (TRACE)HEM EAR DIST
 (TRACE)HEM EAR PROX

CECUM (MILD)PARASITIC INFESTATION

TISSUE << NEUROPSY MEMOS >>
 NO NECROPSY MEMOS RECORDED ON ANIMAL

TISSUE DISTRIBUTION (SEVERITY) << PATHOLOGY OBSERVATIONS >>
 SK EAR DIST NOT SPECIFIED(MODERATE)

SK EAR ARTERY NOT SPECIFIED(MODERATE)

SK THORAX NOT SPECIFIED(MILD)
 NOT SPECIFIED(MILD)
 NOT SPECIFIED(MILD)

NOT SPECIFIED(PRESENT)

HISTOPATHOLOGIC DIAGNOSES / SPECIAL HISTOLOGICAL COMMENTS

HEMORRHAGE
 HEHORRHAGE
 HEHORRHAGE
 HEMORRHAGE
 ACUTE DERMATITIS
 ACUTE MYOSITIS
 SKELETAL MUSCLE DEGENERATION

Appendix F (cont.): PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH DIV OF RES SUPP, PATH SERV GP PRESIDIO OF SAN FRANCISCO, CA 94129 RABBIT/NEW ZEALAND WHITE		INDIVIDUAL ANIMAL DATA DUMP TABLE	PRINTED: 14-DEC-88 PAGE: 29
		STUDY START DATE: 07-JUN-88	ACUTE/PRIMARY SKIN IRRITATION
ANIMAL: 88F0101R	DAY OF DEATH: 1	STATUS: INTERIM SACRIFICE 1	TERMINAL BODY WEIGHT: 2.9 (KGS)
		<< CROSS OBSERVATIONS >> GROSS FREE-TEXT COMMENTS	
TISSUE (SEVERITY)KEYWORDS			
SKIN	(TRACE)HEM THIGH (MARKED)HEM EAR ART		
SKELETAL MUSCLE	(TRACE)HEM THIGH		
LUNGS	(MILD)PNEUMONIA		
		<< ADHERED TO RIB	
TISSUE		<< NECROPSY MEMOS >> NECROPSY MEMOS	
NO NECROPSY MEMOS RECORDED ON ANIMAL			
		<< PATHOLOGY OBSERVATIONS >>	HISTOPATHOLOGIC DIAGNOSES / SPECIAL HISTOLOGICAL COMMENTS
TISSUE		DISTRIBUTION (SEVERITY)	
SK EAR DIST	NOT SPECIFIED(MODERATE) NOT SPECIFIED(TRACE)		HEMORRHAGE ACUTE DERMATITIS
SK EAR ARTERY	NOT SPECIFIED(MARKED) NOT SPECIFIED(TRACE)		HEMORRHAGE ACUTE DERMATITIS
SK THIGH	NOT SPECIFIED(MODERATE) NOT SPECIFIED(TRACE)		HEMORRHAGE ACUTE DERMATITIS
LUNG	NOT SPECIFIED(PRESENT)		SUBACUTE FIBRINOUS PLEURITIS Most consistent with Pasteurella infection
SK. MUSCLE THIGH	NOT SPECIFIED(MILD)		HEMORRHAGE

APPENDIX F (cont.) : PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH
 DIV OF RES SUPP, PATH SERV GP
 PRESIDIO OF SAN FRANCISCO, CA 94129
 RABBIT/NEW ZEALAND WHITE

INDIVIDUAL ANIMAL DATA DUMP TABLE
 STUDY NUMBER: 88004P

PRINTED: 14-DEC-88

PAGE: 30

ACUTE/PRIMARY SKIN IRRITATION

STUDY START DATE: 07-JUN-88

ANIMAL: 88F0102R DAY OF DEATH: 3 STATUS: INTERIM SACRIFICE 3

TERMINAL BODY WEIGHT: 3.4 (KGS)

TISSUE (SEVERITY)KEYWORDS

<< GROSS OBSERVATIONS >>
 GROSS FREE-TEXT COMMENTS

SKIN

(MILD)HEM EAR ART
 (TRACE)HEM EAR DIST
 (TRACE)HEM EAR PROX

SKELETAL MUSCLE

(TRACE)HEM THIGH
 (MARKED)PARASITIC INFESTATION

CECUM

TISSUE

NO NECROPSY MEMOS RECORDED ON ANIMAL

TISSUE

<< PATHOLOGY DISTRIBUTION (SEVERITY)

SK EAR PROX

NOT SPECIFIED(MILD)
 NOT SPECIFIED(TRACE)

SK EAR ARTERY

NOT SPECIFIED(MARKED)

SK THORAX

NOT SPECIFIED(MARKED)

<< NECROPSY MEMOS >>

NECROPSY MEMOS

<< OBSERVATIONS >> HISTOPATHOLOGIC DIAGNOSES / SPECIAL HISTOLOGICAL COMMENTS

HEMORRHAGE
 SUBACUTE DERMATITIS
 HEMORRHAGE
 HEMORRHAGE

Appendix F (cont.) : PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH DIV OF RES SUPP, PATH SERV GP PRESIDIO OF SAN FRANCISCO, CA 94129 RABBIT/NEW ZEALAND WHITE		INDIVIDUAL ANIMAL DATA DUMP TABLE STUDY NUMBER: 88004P		PRINTED: 14-DEC-88 PAGE: 31	
		STUDY START DATE: 07-JUN-88		ACUTE/PRIMARY SKIN IRRITATION	
ANIMAL: 88F0103R		DAY OF DEATH:	4	STATUS: FINAL SACRIFICE	TERMINAL BODY WEIGHT: 3.2 (KGS)
TISSUE (SEVERITY)KEYWORDS		<< GROSS OBSERVATIONS >>		GROSS FREE TEXT COMMENTS	
SKIN (TRACE)HEM EAR ART (TRACE)HEM EAR PROX		.		.	
CECUM (MARKED)PARASITIC INFESTATION		.		.	
TISSUE NO NECROPSY MEMOS RECORDED ON ANIMAL		<< NECROPSY MEMOS >>		NECROPSY MEMOS	
TISSUE		<< PATHOLOGY DISTRIBUTION (SEVERITY)		OBSERVATIONS / HISTOPATHOLOGIC DIAGNOSES / SPECIAL HISTOLOGICAL COMMENTS	
SK EAR DIST		NOT SPECIFIED(TRACE)		SUBACUTE DERMATITIS	
SK EAR PROX		NOT SPECIFIED(MODERATE)		HEMORRHAGE	
SK EAR ARTERY		NOT SPECIFIED(TRACE)		SUBACUTE DERMATITIS	
SK THIGH		NOT SPECIFIED(MILD) NOT SPECIFIED(TRACE)		HEMORRHAGE ACUTE DERMATITIS	
		NOT SPECIFIED(TRACE)		HEMORRHAGE	

Appendix F (cont.) : PATHOLOGY REPORT

LETTERTMAN ARMY INSTITUTE OF RESEARCH
 DIV OF RES SUPP, PATH SERV GP
 PRESIDIO OF SAN FRANCISCO, CA 94129
 RABBIT/NEW ZEALAND WHITE

PRINTED: 14-DEC-88

PAGE: 33

INDIVIDUAL ANIMAL DATA DUMP TABLE

STUDY NUMBER: 88004P

STUDY START DATE: 07-JUN-88

ACUTE/PRIMARY SKIN IRRITATION

ANIMAL: 88F0110R DAY OF DEATH: 1 STATUS: INTERIM SACRIFICE 1

TERMINAL BODY WEIGHT: 3.5 (KGS)

TISSUE (SEVERITY)KEYWORDS

<< GROSS OBSERVATIONS >>
 GROSS FREE-TEXT COMMENTS

SKIN (MILD)HEM EAR ART

(TRACE)HEM THIGH

(MARKED)HEM THORAX

<< NECROPSY MEMOS >>

TISSUE NO NECROPSY MEMOS RECORDED ON ANIMAL

TISSUE DISTRIBUTION (SEVERITY) << PATHOLOGY OBSERVATIONS >>
 STOPATHOLOGIC DIAGNOSES / SPECIAL HISTIOLOGICAL COMMENTS

SK EAR DIST NOT SPECIFIED(TRACE)

HEMORRHAGE

SX EAR PROX NOT SPECIFIED(TRACE)

HEMORRHAGE

NOT SPECIFIED(TRACE)

ACUTE DERMATITIS

NOT SPECIFIED(PRESENT)

ULCERATIVE DERMATITIS

SK EAR ARTERY NOT SPECIFIED(MODERATE)

HEMORRHAGE

NOT SPECIFIED(MODERATE)

ACUTE DERMATITIS

NOT SPECIFIED(PRESENT)

ULCERATIVE DERMATITIS

SX THIGH NOT SPECIFIED(MILD)

HEMORRHAGE

NOT SPECIFIED(MILD)

ACUTE DERMATITIS

NOT SPECIFIED(MILD)

ACUTE MYOSITIS

Appendix F (cont.) : PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH
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 PRESIDIO OF SAN FRANCISCO, CA 94129

RABBIT/NEW ZEALAND WHITE

PRINTED: 14-DEC-88
 INDIVIDUAL ANIMAL DATA DUMP TABLE
 PAGE: 34
 STUDY NUMBER: 880004-P

STUDY START DATE: 07-JUN-88 ACUTE/PRIMARY SKIN IRRITATION

ANIMAL: 88F011R	DAY OF DEATH: 2	STATUS: INTERIM SACRIFICE 2	TERMINAL BODY WEIGHT: 3.4 (KGS)
		<< G R O S S O B S E R V A T I O N S >> GROSS FREE-TEXT COMMENTS	
(SEVERITY)KEYWORDS			
SKIN	(TRACE)HEM EAR ART (TRACE)HEM EAR DIST (TRACE)HEM THORAX		
SKELETAL MUSCLE	(TRACE)HEM THIGH		
		<< N E C R O P S Y M E M O S >> NECROPSY MEMOS	
NO NECROPSY MEMOS RECORDED ON ANIMAL			
TISSUE	DISTRIBUTION (SEVERITY)	PATHOLOGY	O B S E R V A T I O N S HISTOPATHOLOGIC DIAGNOSES / SPECIAL HISTOLOGICAL COMMENTS
SK EAR DIST	NOT SPECIFIED(MODERATE) NOT SPECIFIED(TRACE)		HEMORRHAGE ACUTE DERMATITIS
SK EAR PROX	NOT SPECIFIED(TRACE) NOT SPECIFIED(TRACE)		HEMORRHAGE ACUTE DERMATITIS
SK EAR ARTERY	NOT SPECIFIED(MILD) NOT SPECIFIED(TRACE)		HEMORRHAGE ACUTE DERMATITIS
SK THORAX	NOT SPECIFIED(PRESENT)		SKELETAL MUSCLE DEGENERATION

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RABBIT/NEW ZEALAND WHITE

APPENDIX F (cont.) : PATHOLOGY REPORT

INDIVIDUAL ANIMAL DATA DUMP TABLE
STUDY NUMBER: 88004P

PRINTED: 14-DEC-88
PAGE: 35

STUDY START DATE: 07-JUN-88

ACUTE/PRIMARY SKIN IRRITATION

ANIMAL: 88F0115R DAY OF DEATH: 3 STATUS: INTERIM SACRIFICE 3

TERMINAL BODY WEIGHT: 3.1 (KGS)

(SEVERITY)KEYWORDS << GROSS OBSERVATIONS >>

SKIN (TRACE)HEM EAR ART
(MILD)HEM THORAX
CECUM
(MODERATE)PARASITIC INFESTATION

GROSS FREE-TEXT COMMENTS

TISSUE

SK EAR DIST

SK EAR PROX

SK EAR ARTERY

SK THORAX

CECUM

(MODERATE)PARASITIC INFESTATION

TISSUE

NO NECROPSY MEMOS

<< NECROPSY MEMOS >>

NO NECROPSY MEMOS RECORDED ON ANIMAL

TISSUE

DISTRIBUTION (SEVERITY)

<< PATHOLOGY OBSERVATIONS >>

HISTOPATHOLOGIC DIAGNOSES / SPECIAL HISTOLOGICAL COMMENTS

SK EAR DIST

NOT SPECIFIED(MILD)

HEMORRHAGE

SK EAR PROX

NOT SPECIFIED(MILD)

HEMORRHAGE

SK EAR ARTERY

NOT SPECIFIED(MILD)

HEMORRHAGE

SK THORAX

NOT SPECIFIED(MILD)

ACUTE MYOSITIS

NOT SPECIFIED(PRESENT)

SKELETAL MUSCLE DEGENERATION

Appendix F (cont.): PATHOLOGY REPORT

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 DIV OF RES SUPP, PATH SERV GP
 PRESIDIO OF SAN FRANCISCO, CA 94129
 RABBIT/NEW ZEALAND WHITE

ANIMAL: 88F0116R DAY OF DEATH: 4 STATUS: FINAL SACRIFICE

(SEVERITY)KEYWORDS

SKIN (TRACE)HEM EAR ART
 (TRACE)HEM EAR DIST
 (TRACE)HEM EAR PROX
 (MILD)HEM THORAX
 (MODERATE)ALOPECIA
 CECUM (MILD)PARASITIC INFESTATION

TISSUE NO NECROPSY MEMOS

NO NECROPSY MEMOS RECORDED ON ANIMAL

INDIVIDUAL ANIMAL DATA DUMP TABLE
 STUDY NUMBER: 88004P

STUDY START DATE: 07-JUN-88

PRINTED: 14-DEC-88
 PAGE: 36

ACUTE/PRIMARY SKIN IRRITATION

TERMINAL BODY WEIGHT: 3.6 (KGS)

<< GROSS OBSERVATIONS >>

GROSS FREE-TEXT COMMENTS

<< NECROPSY MEMOS >>
 NECROPSY MEMOS

TISSUE DISTRIBUTION (SEVERITY)

SK EAR DIST NOT SPECIFIED(MILD)
 SK EAR PROX NOT SPECIFIED(PRESENT)
 SK EAR ARTERY NOT SPECIFIED(MODERATE)
 NOT SPECIFIED(MILD)
 NOT SPECIFIED(MILD)

TISSUE

<< PATHOLOGY OBSERVATIONS >>

HISTOPATHOLOGIC DIAGNOSES / SPECIAL HISTOLOGICAL COMMENTS

ACUTE DERMATITIS
 MONONUCLEAR CELL INFILTRATION
 HEMORRHAGE
 ACUTE DERMATITIS
 HEMORRHAGE

Appendix F (cont.) : PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH DIV OF RES SUPP, PATH SERV GP PRESIDIO OF SAN FRANCISCO, CA 94129 RABBIT/NEW ZEALAND WHITE		INDIVIDUAL ANIMAL DATA DUMP TABLE STUDY NUMBER: 880004P	PRINTED: 14-DEC-88 PAGE: 37
		STUDY START DATE: 07-JUN-88	ACUTE/PRIMARY SKIN IRRITATION
ANIMAL: 88F0093L	DAY OF DEATH: 2	STATUS: INTERIM SACRIFICE 2	TERMINAL BODY WEIGHT: 3.2 (KGS)
TISSUE	(SEVERITY)KEYWORDS	<< GROSS OBSERVATIONS >>	GROSS FREE-TEXT COMMENTS
SKIN	(TRACE)HEM EAR ART (TRACE)HEM EAR DIST (TRACE)HEM EAR PROX	<< NECROPSY MEMOS >>	
TISSUE	<< NECROPSY MEMOS >>		
NO NECROPSY MEMOS RECORDED ON ANIMAL			
TISSUE	DISTRIBUTION (SEVERITY)	<< PATHOLOGY OBSERVATIONS >>	
SK EAR DIST	NOT SPECIFIED(MODERATE) NOT SPECIFIED(TRACE)	HISTOPATHOLOGIC DIAGNOSES / SPECIAL HISTOLOGICAL COMMENTS	
SK EAR PROX	NOT SPECIFIED(MILD)	HEMORRHAGE ACUTE DERMATITIS	
SK EAR ARTERY	NOT SPECIFIED(MODERATE) NOT SPECIFIED(TRACE)	HEMORRHAGE	
SK THORAX	NOT SPECIFIED(MILD)	HEMORRHAGE ACUTE DERMATITIS	
SK THIGH	NOT SPECIFIED(PRESENT)	ACUTE DERMATITIS ULCERATIVE DERMATITIS	

Appendix F (cont.): PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH
 DIV OF RES SUPP, PATH SERV GP
 PRESIDIO OF SAN FRANCISCO, CA 94129
 RABBIT/NEW ZEALAND WHITE

INDIVIDUAL ANIMAL DATA DUMP TABLE
 STUDY NUMBER: 88004/P

STUDY START DATE: 07-JUN-88

ANIMAL: R⁺0094L DAY OF DEATH: 2 STATUS: INTERIM SACRIFICE 2 TERMINAL BODY WEIGHT: 3.1 (KGS)

PRINTED: 14-DEC-88
 PAGE: 38

ACUTE/PRIMARY SKIN IRRITATION

TISSUE (SEVERITY)KEYWORDS << GROSS OBSERVATIONS >>
 GROSS FREE-TEXT COMMENTS

SKIN (TRACE)HEM EAR ART

SKELETAL MUSCLE (TRACE)HEM THIGH

EAR (MILD)OTITIS EXTERNA

TISSUE << NECROPSY MEMOS >>
 NECROPSY MEMOS

NO NECROPSY MEMOS RECORDED ON ANIMAL

TISSUE	DISTRIBUTION (SEVERITY)	PATHOLOGY	OBSERVATIONS HISTOPATHOLOGIC DIAGNOSES / SPECIAL HISTOLOGICAL COMMENTS
SK EAR DIST	NOT SPECIFIED(MILD)		HEMORRHAGE
SK EAR ARTERY	NOT SPECIFIED(MODERATE)		HEMORRHAGE ACUTE DERMATITIS
SK THIGH	NOT SPECIFIED(TRACE)		HEMORRHAGE
EAR DEBRIS	NOT SPECIFIED(PRESENT)		FIBRINOCELLULAR EXUDATE

Appendix F (cont.) : PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH DIV OF RES SUPP, PATH SERV GP PRESIDIO OF SAN FRANCISCO, CA 94129 RABBIT/NEW ZEALAND WHITE		INDIVIDUAL ANIMAL DATA DUMP TABLE STUDY NUMBER: 88004.p		PRINTED: 14-DEC-88 PAGE: 39	
		STUDY START DATE: 07-JUN-88		ACUTE/PRIMARY SKIN IRRITATION	
ANIMAL: 88F0098L	DAY OF DEATH: 4	STATUS: FINAL SACRIFICE	TERMINAL BODY WEIGHT: 3.2 (KGS)		
		<< G R O S S O B S E R V A T I O N S >>	GROSS FREE-TEXT COMMENTS		
TISSUE	(SEVERITY)KEYWORDS				
CECUM	(MILD)PARASITIC INFESTATION				
SKIN	(MILD)FOLLICULITIS				
			SUB-MANDIBULAR		
TISSUE		<< N E C R O P S Y M E M O S >>	NECROPSY MEMOS		
NO NECROPSY MEMOS RECORDED ON ANIMAL					
TISSUE	DISTRIBUTION (SEVERITY)	<< P A T H O L O G Y O B S E R V A T I O N S >>	HISTOPATHOLOGIC DIAGNOSES / SPECIAL HISTOLOGICAL COMMENTS		
SK EAR DIST	NOT SPECIFIED(TRACE) NOT SPECIFIED(MILD)				
SK EAR PROX	NOT SPECIFIED(MILD) NOT SPECIFIED(TRACE)				
SK EAR ARTERY	NOT SPECIFIED(TRACE)				
SK THIGH	NOT SPECIFIED(TRACE)				
			HEMORRHAGE ACUTE DERMATITIS		
			HEMORRHAGE		
			ACUTE DERMATITIS		
			HEMORRHAGE		
			HEMORRHAGE		
			HEMORRHAGE		

Appendix F (cont.) : PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH
 DIV OF RES SUPP, PATH SERV GP
 PRESIDIO OF SAN FRANCISCO, CA 94129
 RABBIT/NEW ZEALAND WHITE

INDIVIDUAL ANIMAL DATA DUMP TABLE
 STUDY NUMBER: 880004P

STUDY START DATE: 07-JUN-88

ACUTE/PRIMARY SKIN IRRITATION

ANIMAL: 88F0099L DAY OF DEATH: 3 STATUS: INTERIM SACRIFICE 3 TERMINAL BODY WEIGHT: 3.5 (KGS)

TISSUE (SEVERITY)KEYWORDS << G R O S S O B S E R V A T I O N S >>
 SKIN (MILD)HEM EAR ART GROSS FREE-TEXT COMMENTS

(TRACE)HEM EAR DIST
 (TRACE)HEM EAR PROX

CECUM (MILD)PARASITIC INFESTATION

TISSUE << N E C R O P S Y M E M O S >>
 NO NECROPSY MEMOS RECORDED ON ANIMAL

TISSUE DISTRIBUTION (SEVERITY) << P A T H O L O G Y O B S E R V A T I O N S >>
 SK EAR DIST NOT SPECIFIED(TRACE) HEMORRHAGE
 SK EAR ARTERY NOT SPECIFIED(MILD) HEMORRHAGE
 SK THORAX NOT SPECIFIED(MARKED) HEMORRHAGE
 NOT SPECIFIED(TRACE) ACUTE DERMATITI

Appendix F (cont.): PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH
 DIV OF RES SUPP, PATH SERV GP
 PRESIDIO OF SAN FRANCISCO, CA 94129
 RABBIT/NEW ZEALAND WHITE

INDIVIDUAL ANIMAL DATA DUMP TABLE
 STUDY NUMBER: 88004P
 PRINTED: 14-DEC-88
 PAGE: 41

STUDY START DATE: 07-JUN-88

ACUTE/PRIMARY SKIN IRRITATION

ANIMAL: 88F0101L DAY OF DEATH: 1 STATUS: INTERIM SACRIFICE 1

TERMINAL BODY WEIGHT: 2.9 (KGS)

TISSUE (SEVERITY)KEYWORDS << GROSS OBSERVATIONS >>

GROSS FREE-TEXT COMMENTS

SKIN (MODERATE)HEM EAR ART

(TRACE)HEM THIGH

LUNGS (MILD)PNEUMONIA ADHERED TO RIB

TISSUE << NECROPSY MEMOS >>

NECROPSY MEMOS

NO NECROPSY MEMOS RECORDED ON ANIMAL

TISSUE DISTRIBUTION (SEVERITY) << PATHOLOGY OBSERVATIONS >>

HISTOPATHOLOGIC DIAGNOSES / SPECIAL HISTOLOGICAL COMMENTS

SK EAR DIST NOT SPECIFIED(WILD) HEMORRHAGE

SK EAR PROX NOT SPECIFIED(MODERATE) HEMORRHAGE

NOT SPECIFIED(TRACE) ACUTE DERMATITIS

SK EAR ARTERY NOT SPECIFIED(MODERATE) HEMORRHAGE

NOT SPECIFIED(TRACE) ACUTE DERMATITIS

LUNG NOT SPECIFIED(PRESENT) SUBACUTE FIBRINOUS PLEURITIS

SUBACUTE FIBRINOUS PLEURITIS

Most consistent with *Pasteurella* infection

Appendix F (cont.) : PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH
 DIV OF RES SUPP, PATH SERV GP
 PRESIDIO OF SAN FRANCISCO, CA 94129
 RABBIT/NEW ZEALAND WHITE

STUDY START DATE: 07-JUN-88 ACUTE/PRIMARY SKIN IRRITATION

ANIMAL: 88F0102L DAY OF DEATH: 3 STATUS: INTERIM SACRIFICE 3 TERMINAL BODY WEIGHT: 3.4 (KGS)

TISSUE (SEVERITY)KEYWORDS

SKIN ((MILD)HEM EAR ART

CECUM ((MARKED)PARASITIC INFESTATION

TISSUE NO NECROPSY MEMOS RECORDED ON ANIMAL

TISSUE DISTRIBUTION (SEVERITY)

SK EAR DIST NOT SPECIFIED(TRACE)

SK EAR PROX NOT SPECIFIED(MODERATE)

SK EAR ARTERY NOT SPECIFIED(TRACE)

NOT SPECIFIED(MODERATE)

INDIVIDUAL ANIMAL DATA DUMP TABLE
 STUDY NUMBER: 88004P

PRINTED: 14-DEC-88
 PAGE: 42

<< G R O S S O B S E R V A T I O N S >>
 GROSS FREE-TEXT COMMENTS

<< N E C R O P S Y M E M O S >>
 NECROPSY MEMOS

Appendix F (cont.): PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH DIV OF RES SUPP, PATH SERV GP PRESIDIO OF SAN FRANCISCO, CA 94129		INDIVIDUAL ANIMAL DATA DUMP TABLE STUDY NUMBER: 88004P		PRINTED: 14-DEC-88 PAGE: 43
RABBIT/NEW ZEALAND WHITE		STUDY START DATE: 07-JUN-88		ACUTE/PRIMARY SKIN IRRITATION
ANIMAL: 88F0103L	DAY OF DEATH: 4	STATUS: FINAL SACRIFICE		TERMINAL BODY WEIGHT: 3.2 (KGS)
TISSUE (SEVERITY)KEYWORDS	<< G R O S S (TRACE)HEM EAR ART	O B S E R V A T I O N S >> (MARKED)PARASITIC INFESTATION		GROSS FREE-TEXT COMMENTS
SKIN CECUM				
TISSUE		<< N E C R O P S Y M E M O S >>	NECROPSY MEMOS	
NO NECROPSY MEMOS RECORDED ON ANIMAL				
TISSUE	DISTRIBUTION (SEVERITY)	PATHOLOGY	O B S E R V A T I O N S HISTOPATHOLOGIC DIAGNOSES / SPECIAL HISTOLOGICAL COMMENTS	
SK EAR ARTERY	NOT SPECIFIED(TRACE) NOT SPECIFIED(MILD)		HEMORRHAGE ACUTE DERMATITIS	

Appendix F (cont.) : PATHOLOGY REPORT

LETERMAN ARMY INSTITUTE OF RESEARCH
 DIV OF RES SUPP, PATH SERV GP
 PRESIDIO OF SAN FRANCISCO, CA 94129
 RABBIT/NEW ZEALAND WHITE

INDIVIDUAL ANIMAL DATA DUMP TABLE
 STUDY NUMBER: 88004P

STUDY START DATE: 07-JUN-88

ACUTE/PRIMARY SKIN IRRITATION

ANIMAL:	88F0108L	DAY OF DEATH:	1	STATUS:	INTERIM SACRIFICE 1	TERMINAL BODY WEIGHT:	3.6 (KGS)
TISSUE				<< GROSS OBSERVATIONS >>	GROSS FREE-TEXT COMMENTS		
SKIN				(TRACE)HEM EAR ART			
SKELETAL MUSCLE				(MILD)HEM THIGH			
LYMPH NODES				(TRACE)HEM THORAX			
				(MODERATE)ABCESS(ES)	PASTEURELLA		
TISSUE				<< NECROPSY MEMOS >>	NECROPSY MEMOS		
NO NECROPSY MEMOS RECORDED ON ANIMAL							
TISSUE				<< PATHOLOGY OBSERVATIONS >>	HISTOPATHOLOGIC DIAGNOSES / SPECIAL HISTOLOGICAL COMMENTS		
SK EAR DIST				NOT SPECIFIED(MILD)	HEMORRHAGE		
				NOT SPECIFIED(TRACE)	ACUTE DERMATITIS		
SK EAR PROX				NOT SPECIFIED(MILD)	HEMORRHAGE		
				NOT SPECIFIED(TRACE)	ACUTE DERMATITIS		
SK EAR ARTERY				NOT SPECIFIED(MILD)	HEMORRHAGE		
				NOT SPECIFIED(TRACE)	ACUTE DERMATITIS		
LYMPH NODE				NOT SPECIFIED(PRESENT)	ABSCSSION		

Appendix F (cont.): PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH
 DIV OF RES SUPP, PATH SERV GP
 PRESIDIO OF SAN FRANCISCO, CA 94129
 RABBIT/NEW ZEALAND WHITE

PRINTED: 14-DEC-88
 STUDY NUMBER: 88004P
 PAGE: 45

STUDY START DATE: 07-JUN-88
 ACUTE/PRIMARY SKIN IRRITATION

ANIMAL: 88F0110L DAY OF DEATH: 1 STATUS: INTERIM SACRIFICE 1
 TISSUE (SEVERITY)KEYWORDS << GROSS OBSERVATIONS >>
 SKIN (TRACE)HEM THIGH
 (MARKED)HEM EAR ART
 TISSUE << NEUROPSY MEMOS >>

NO NECROPSY MEMOS RECORDED ON ANIMAL
 TISSUE << PATHOLOGY OBSERVATIONS >>
 SK EAR DIST NOT SPECIFIED(MILD)
 SK EAR PROX NOT SPECIFIED(TRACE)
 NOT SPECIFIED(TRACE)
 SK EAR ARTERY NOT SPECIFIED(MODERATE)
 NOT SPECIFIED(MODERATE)

HISTOPATHOLOGIC DIAGNOSES / SPECIAL HISTOLOGICAL COMMENTS
 SK EAR DIST HEMORRHAGE
 SK EAR PROX HEMORRHAGE
 ACUTE DERMATITIS
 SK EAR ARTERY HEMORRHAGE
 ACUTE DERMATITIS
 SK THORAX TISSUE IS MISSING

Appendix F (cont.): PATHOLOGY REPORT

PRINTED: 14-DEC-88
 PAGE: 46

INDIVIDUAL ANIMAL DATA DUMP TABLE
 STUDY NUMBER: 88004P

ACUTE/PRIMARY SKIN IRRITATION

STUDY START DATE: 07-JUN-88

TERMINAL BODY WEIGHT: 3.4 (KGS)

ANIMAL: 88F011L DAY OF DEATH: 2 STATUS: INTERIM SACRIFICE 2

<< GROSS OBSERVATIONS >>

GROSS FREE TEXT COMMENTS

(SEVERITY)KEYWORDS

SKIN

(TRACE)HEM EAR ART
 (TRACE)HEM EAR DIST
 (TRACE)HEM EAR PROX

TISSUE

<< NEUROPATHOLOGY MEMOS >>

NEUROPATHOLOGY MEMOS

TISSUE

NO NECROPSY MEMOS RECORDED ON ANIMAL

TISSUE	DISTRIBUTION (SEVERITY)	PATHOLOGY	OBSERVATIONS HISTOPATHOLOGIC DIAGNOSES / SPECIAL HISTOLOGICAL COMMENTS
SK EAR DIST	NOT SPECIFIED(TRACE) NOT SPECIFIED(TRACE)		HEMORRHAGE ACUTE DERMATITIS
SK EAR PROX	NOT SPECIFIED(MILD)		HEMORRHAGE
SK EAR ARTERY	NOT SPECIFIED(MODERATE)		HEMORRHAGE

Appendix F (cont.): PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH
 DIV OF RES SUPP, PATH SERV GP
 PRESIDIO OF SAN FRANCISCO, CA 94129
 RABBIT/NEW ZEALAND WHITE

ANIMAL: 88F015L DAY OF DEATH: 3

STUDY START DATE: 07-JUN-88

INDIVIDUAL ANIMAL DATA DUMP TABLE
 STUDY NUMBER: 88004PPRINTED: 14-DEC-88
 PAGE: 47

ACUTE/PRIMARY SKIN IRRITATION

STATUS: INTERIM SACRIFICE 3

TERMINAL BODY WEIGHT: 3.1 (KGS)

<< GROSS OBSERVATIONS >>

GROSS FREE-TEXT COMMENTS

(SEVERITY)KEYWORDS

SKIN

(TRACE)HEM EAR DIST

(MILD)HEM THORAX

(TRACE)HEM EAR ART

(MODERATE)PARASITIC INFESTATION

<< NECROPSY MEMOS >>

NECROPSY MEMOS

TISSUE

NO NECROPSY MEMOS RECORDED ON ANIMAL

DISTRIBUTION (SEVERITY)

<< PATHOLOGY OBSERVATIONS >>

HISTOPATHOLOGIC DIAGNOSES / SPECIAL HISTOLOGICAL COMMENTS

SK EAR DIST

NOT SPECIFIED(MILD)

HEMORRHAGE

SK EAR PROX

NOT SPECIFIED(MILD)

HEMORRHAGE

SK EAR ARTERY

NOT SPECIFIED(MILD)

HEMORRHAGE

SK THORAX

NOT SPECIFIED(TRACE)

SUBACUTE DERMATITIS

CECUM

NOT SPECIFIED(MODERATE)

HEMORRHAGE

<< PATHOLOGY

HISTOPATHOLOGIC DIAGNOSES / SPECIAL HISTOLOGICAL COMMENTS

SK THORAX

NOT SPECIFIED(MODERATE)

HEMORRHAGE

SK LIVER

NOT SPECIFIED(MODERATE)

HEMORRHAGE

SK SPLEEN

NOT SPECIFIED(MODERATE)

HEMORRHAGE

SK KIDNEY

NOT SPECIFIED(MODERATE)

HEMORRHAGE

SK BLADDER

NOT SPECIFIED(MODERATE)

HEMORRHAGE

SK BRAIN

NOT SPECIFIED(MODERATE)

HEMORRHAGE

SK MUSCLE

NOT SPECIFIED(MODERATE)

HEMORRHAGE

SK LUNG

NOT SPECIFIED(MODERATE)

HEMORRHAGE

SK STOMACH

NOT SPECIFIED(MODERATE)

HEMORRHAGE

SK INTESTINE

NOT SPECIFIED(MODERATE)

HEMORRHAGE

SK PANCREAS

NOT SPECIFIED(MODERATE)

HEMORRHAGE

SK ADRENAL

NOT SPECIFIED(MODERATE)

HEMORRHAGE

SK TESTIS

NOT SPECIFIED(MODERATE)

HEMORRHAGE

SK OVARY

NOT SPECIFIED(MODERATE)

HEMORRHAGE

SK UTERUS

NOT SPECIFIED(MODERATE)

HEMORRHAGE

SK BLADDER

NOT SPECIFIED(MODERATE)

HEMORRHAGE

SK LIVER

NOT SPECIFIED(MODERATE)

HEMORRHAGE

SK SPLEEN

NOT SPECIFIED(MODERATE)

HEMORRHAGE

SK KIDNEY

NOT SPECIFIED(MODERATE)

HEMORRHAGE

SK BLADDER

NOT SPECIFIED(MODERATE)

HEMORRHAGE

SK LUNG

NOT SPECIFIED(MODERATE)

HEMORRHAGE

SK STOMACH

NOT SPECIFIED(MODERATE)

HEMORRHAGE

SK INTESTINE

NOT SPECIFIED(MODERATE)

HEMORRHAGE

SK PANCREAS

NOT SPECIFIED(MODERATE)

HEMORRHAGE

SK ADRENAL

NOT SPECIFIED(MODERATE)

HEMORRHAGE

SK TESTIS

NOT SPECIFIED(MODERATE)

HEMORRHAGE

SK OVARY

NOT SPECIFIED(MODERATE)

HEMORRHAGE

SK UTERUS

NOT SPECIFIED(MODERATE)

HEMORRHAGE

APPENDIX F (cont.); PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH DIV OF RES SUPP, PATH SERV GP PRESIDIO OF SAN FRANCISCO, CA 94129 RABBIT/NEW ZEALAND WHITE		PRINTED: 14-DEC-88 PAGE: 48
		ACUTE/PRIMARY SKIN IRRITATION
ANIMAL: 88F0116L	DAY OF DEATH: 4	STUDY START DATE: 07-JUN-88
		TERMINAL BODY WEIGHT: 3.6 (KGS)
(SEVERITY)KEYWORDS		<< G R O S S O B S E R V A T I O N S >> GROSS FREE-TEXT COMMENTS
SKIN	(TRACE)HEM EAR ART (TRACE)HEM THORAX (TRACE)HEM THIGH (MODERATE)ALOPECIA	DORSAL ANTERIOR THORAX
CECUM	(MILD)PARASITIC INFESTATION	<< N E C R O P S Y M E M O S >> NECROPSY MEMOS
TISSUE	NO NECROPSY MEMOS RECORDED ON ANIMAL	
TISSUE	DISTRIBUTION (SEVERITY)	<< P A T H O L O G Y O B S E R V A T I O N S >> HISTOPATHOLOGIC DIAGNOSES / SPECIAL HISTOLOGICAL COMMENTS
SK EAR DIST	NOT SPECIFIED(TRACE)	ACUTE DERMATITIS
SK EAR PROX	NOT SPECIFIED(TRACE)	HEMORRHAGE
SK EAR ARTERY	NOT SPECIFIED(MODERATE) NOT SPECIFIED(MILD)	HEMORRHAGE SUBACUTE DERMATITIS
SK THORAX	NOT SPECIFIED(TRACE)	HEMORRHAGE

Zaucha et al--112

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